

Figure 1A

Figure 1B

Figure 1C

Figure 1D

Figure 1E

Figure 1r

26
 A V I N I O A P K G L A F T O V D O S I K I A U E S P O C O V S A V A V I V S
 TGCAGTAAACCACTGATTCGGCTTAACACTGACTCATCTTGATGTCATGTCAGTTCAGTTCAGCTGAGTTTCAGGTACAGGGTACCCCTACCTC
 4810 4820 4830 4840 4850 4860 4870 4880 4890 4900 4910 4920
 S P E O G I M E L L F P A P D C E D I A E L L O G L A P G S E T I V S V V A L H D
 GAGGCTGAGGATGCGATGCGCTATGCGCTATGCGCTATGCGCTATGCGCTATGCGCTATGCGCTATGCGCTATGCGCTATGCGCTATGCGCTA
 4930 4940 4950 4960 4970 4980 4990 5000 5010 5020 5030 5040
 D M E S Q P L I G T O S 27
 T A I P A P I T O L K F T O V I P I S I S A Q W T P P H V
 TGATAGGAGCTACCGCTGATTCGGCTAACCTGATACAGCTTACAGCTTACAGCTTACAGCTTACAGCTTACAGCTTACAGCTTACAGCTTACAGT
 5050 5060 5070 5080 5090 5100 5110 5120 5130 5140 5150 5160
 O L I T G V A V N V T P K E K I G P M K E I M L A P O S S S V V S G L M V A T K
 TCAACTCTGCTGATTCGAGTACCGCTGAGCTGGCTGAGCTGGCTGAGCTGGCTGAGCTGGCTGAGCTGGCTGAGCTGGCTGAGCTGGCTGAG
 5170 5180 5190 5200 5210 5220 5230 5240 5250 5260 5270 5280
 V E V S V V A L K D T L I S A P A Q G V V T I L C W V S P P R A M A R V I O A I E 28
 ATATGAGGCTGCTAIGCTCTAACGAGCTTACAGGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAAC
 5290 5300 5310 5320 5330 5340 5350 5360 5370 5380 5390 5400
 T T I T I S V A L K T E T I I G f Q V O A V P A N G Q I P I Q R T I K P D V A S
 GAGGAGCTGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAAC
 5410 5420 5430 5440 5450 5460 5470 5480 5490 5500 5510 5520
 T F I T G L O P G T I O V K I V L V T L W D N A M S S P V V I D A S I A I D A P S
 CTGAGCTGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAAC
 5530 5540 5550 5560 5570 5580 5590 5600 5610 5620 5630 5640
 M L A F L A T T P M S L L V S W O P P A R A R I T G V I I K V E K P G S P P R E V
 CAACCTGCTTCTGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAACGAGCTAAC
 5650 5660 5670 5680 5690 5700 5710 5720 5730 5740 5750

Figure 1C

Figure 1H

Figure 2A

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Pair 1

0 1 5' - ATTCAATATGGAAACAGCAAATGGTTCAAGCCCCAGTCCGGGGCTGTCAGTCAAAGCAGGCCGGGT - 3'
0 2 3' - CTAATACGTCCGGTGCCTTACCAAGTCGGGGTCAACGGACAGTCAGTTCGTTGGGCCAACAAATA - 5'

Pair 2

0 3 5' - GTTATGACAATGGAAAACACTATCAGATAAAATCAACAGTGGAGGCCACCTACCTAGGTAAATGCTTG - 3'
0 4 3' - CTGTTACCTTTTGTGATAGTCTTATTAGTTGTCAACCCCTGGCTGATGGATCCATT - 5'

Pair 3

0 5 5' - GTTTGTACTTTTAGGAGAACGGTTAACTGGAAAGTAAACCTGAAGCT - 3'
0 6 3' - ACACAACCAAACATGAAAAATACCTCCTTCGGTCCAAAATGACGCTTCATTTGGACTTCGACITCTCT - 5'

Pair 4

0 7 5' - GAAGAGACTTGGCTTACAGACTGGGAACACTTACCCGAGTGGGTGACCTTATGGGCTCTTAA - 3'
0 8 3' - GAACCAAAACATGAAAAATGGCTCAACCCACTGIGATAWTCUCAAG - 5'

Figure 2B

Pair 5

09 5' - GACTCCATGATCTGGGACTGTACCTGCCATCGGGGCTGGGGAGGAAATAAGCTGTACC - 3'.
10 GATTTCCTGAGGTACTAGACCCCTGACATGGACCTGCCCCCTCTTATTC - 5'.

11 5' - ATCCCAACGGCTCCATGAAGGGGGTCACTCCCTAACAGATTTGGTGACACCTGGAGGAGACCACTGAGACT - 3'.
12 GACATGGTAAAGCTTGGGACGGTACTTCCCCAAGTCAGGAAGGGCTAACCTGGACCTCTGGTGTACTCTGACCCAA - 5'.

Pair 6

Pair 7

13 5' - CGTGGTTACATGTTAGCTGTCTCTCTCTTACCTGGAAAGGAGAATGGACCTGGAAAGCCATAGCTGAG - 3'.
14 3' - TGTACATTCACACACAGAACCTTAACCTTCTTCTTACCTGGACCTCTTACCTGGAACTCTGACTCTCTAG - 5'.

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Figure 3

Synthesis of F.N. Gene (14 - 472 b.p.)

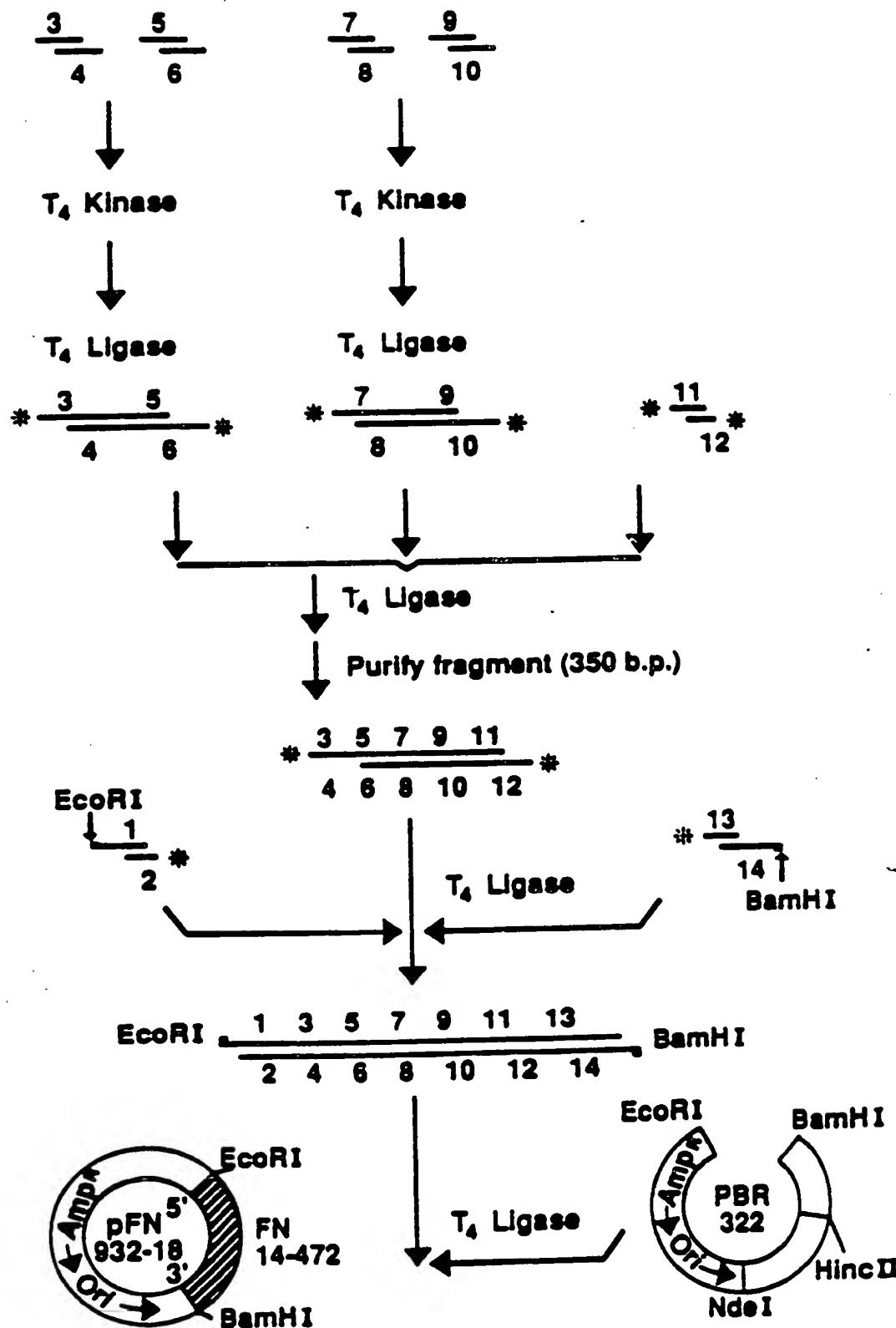


Figure 4

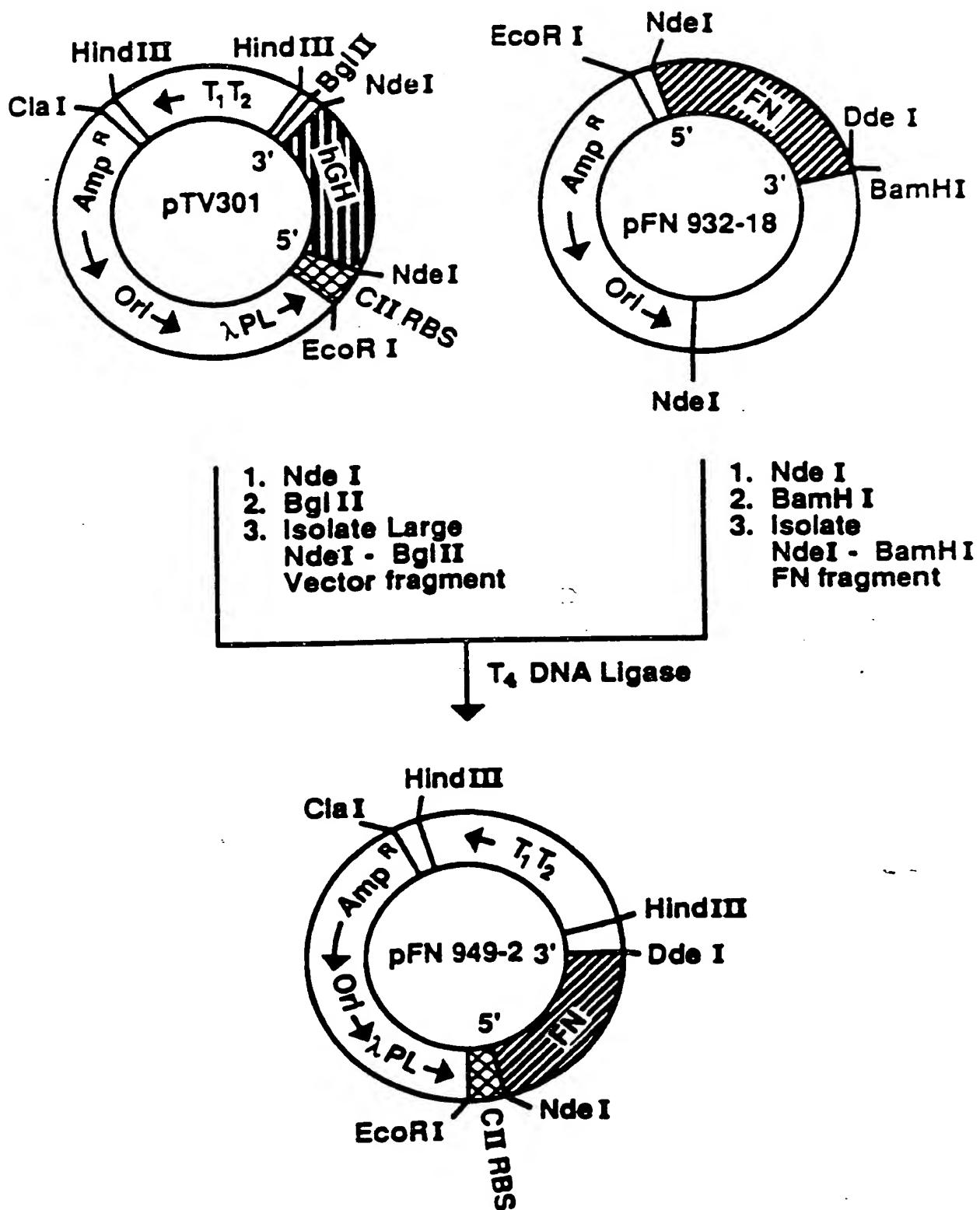


Figure 5

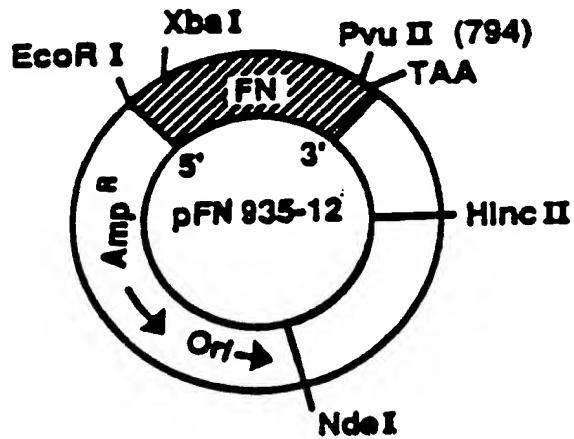
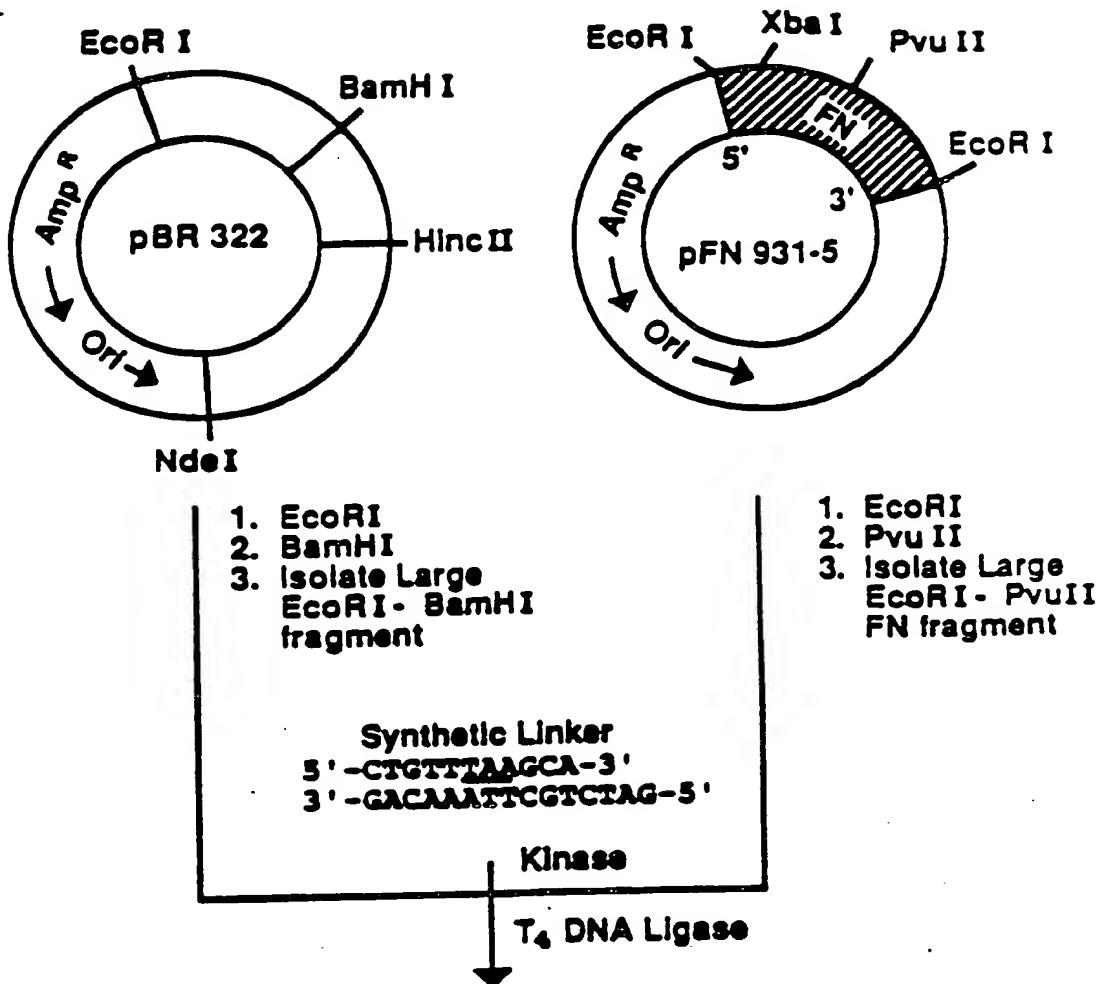


Figure 6

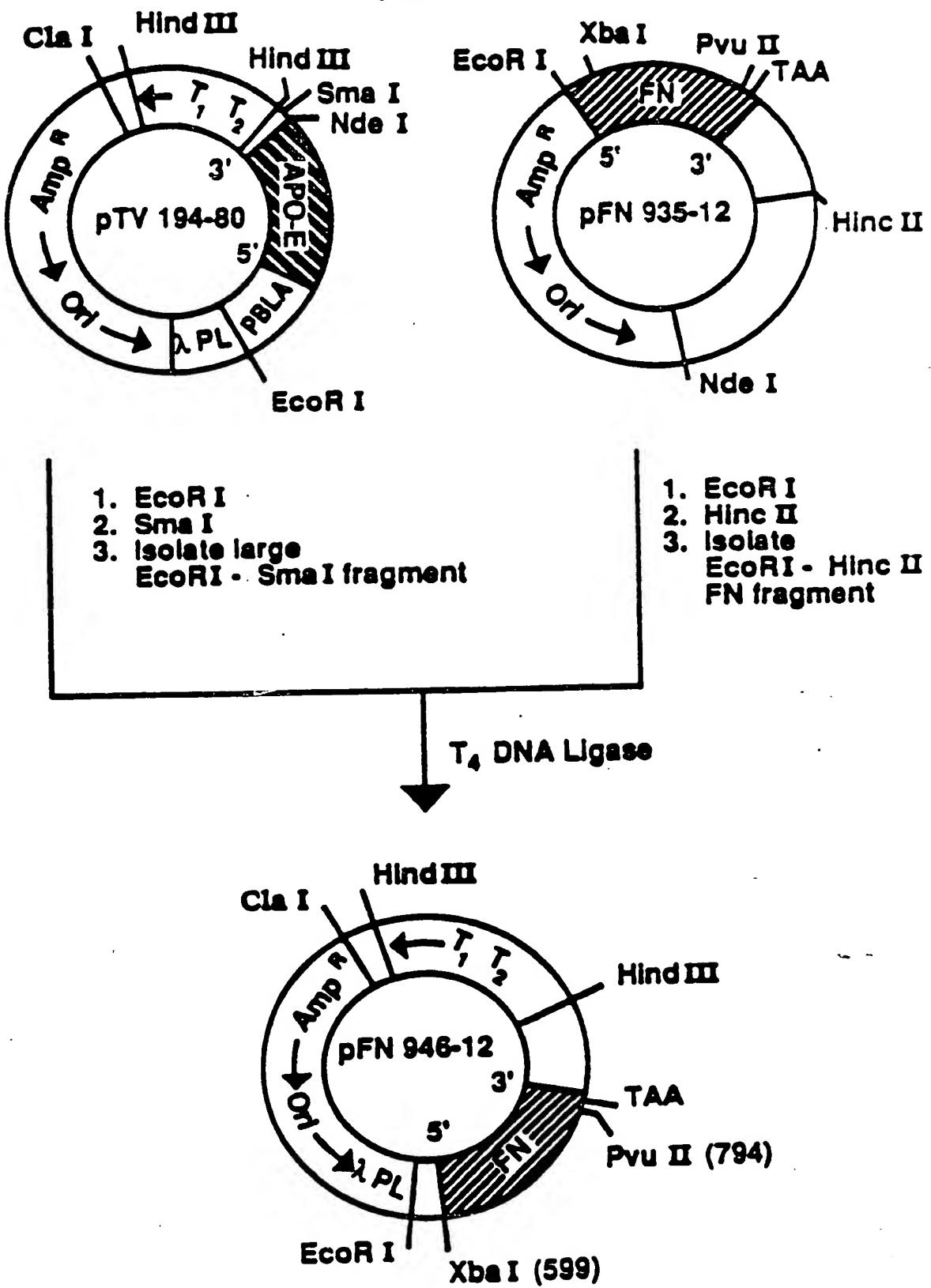


Figure 7

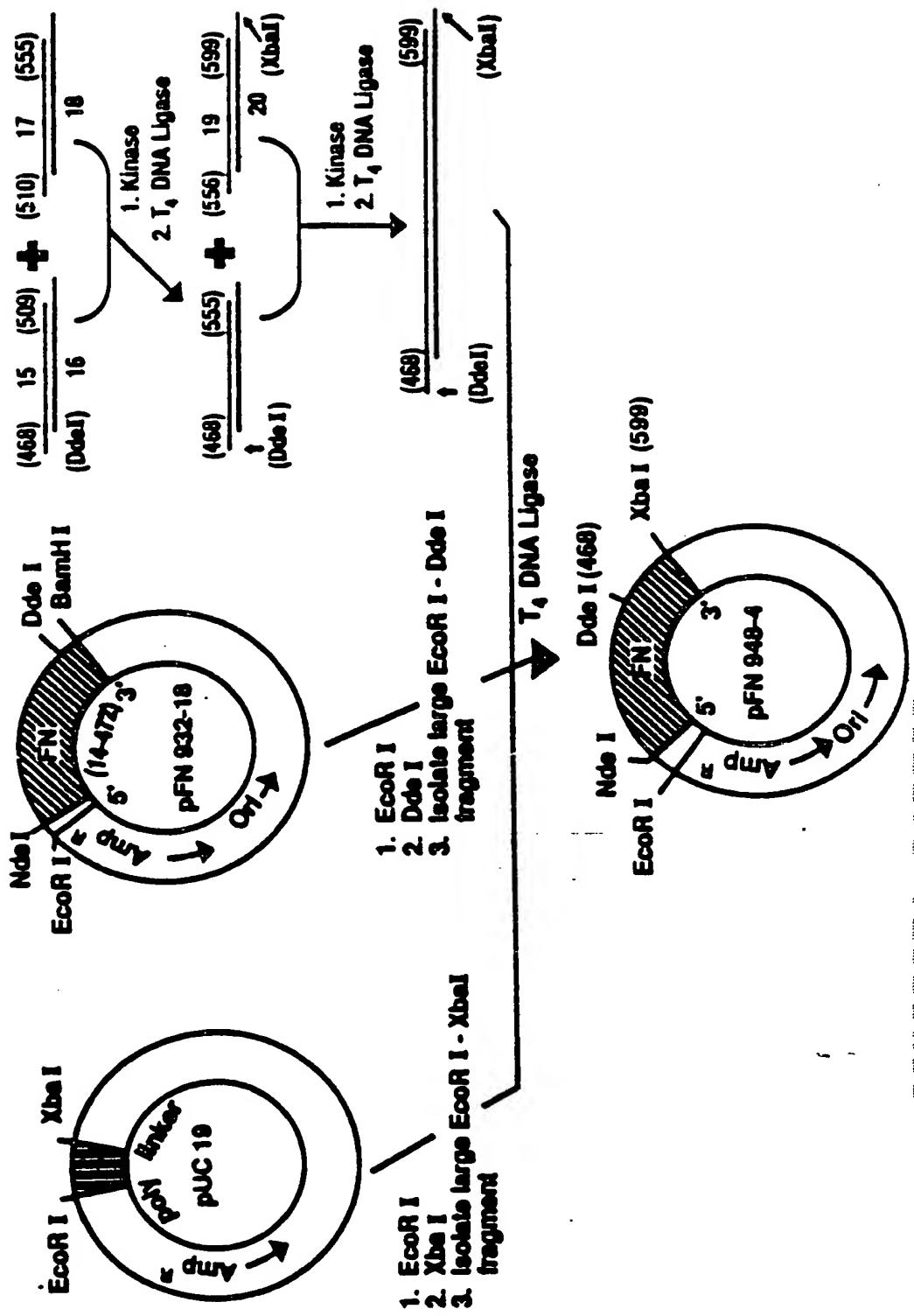
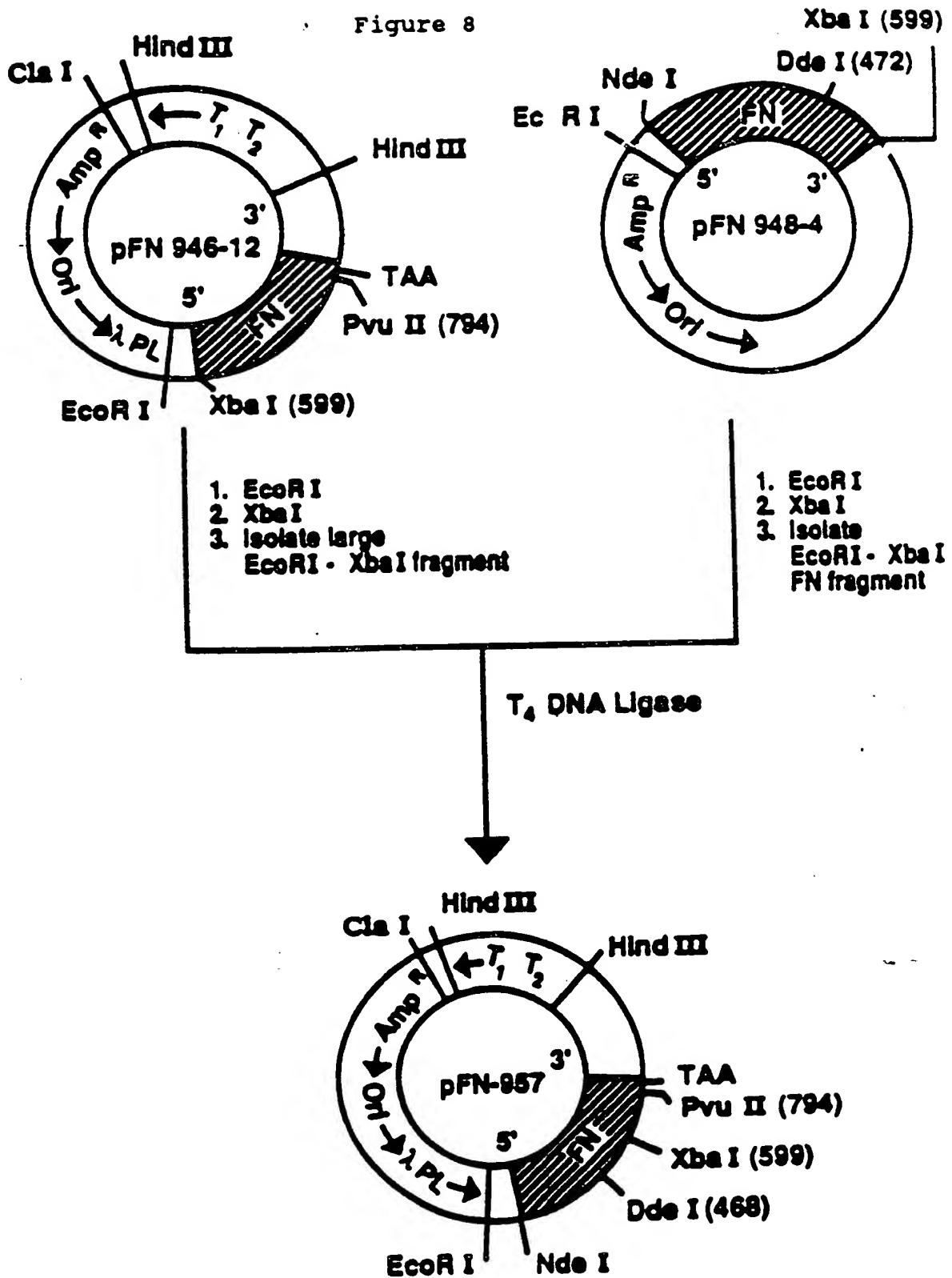


Figure 8

00000000000000000000000000000000



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Figure 9

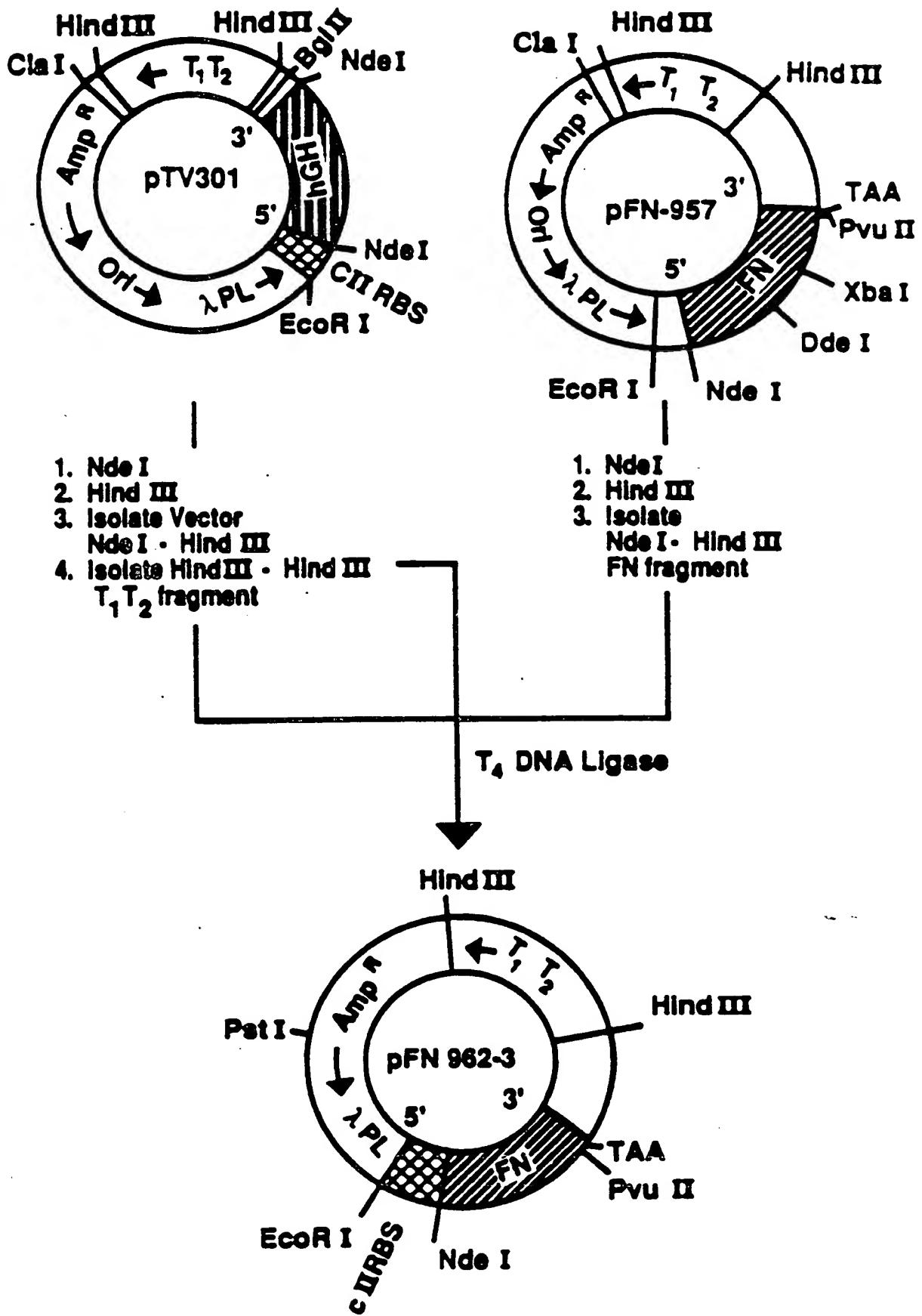
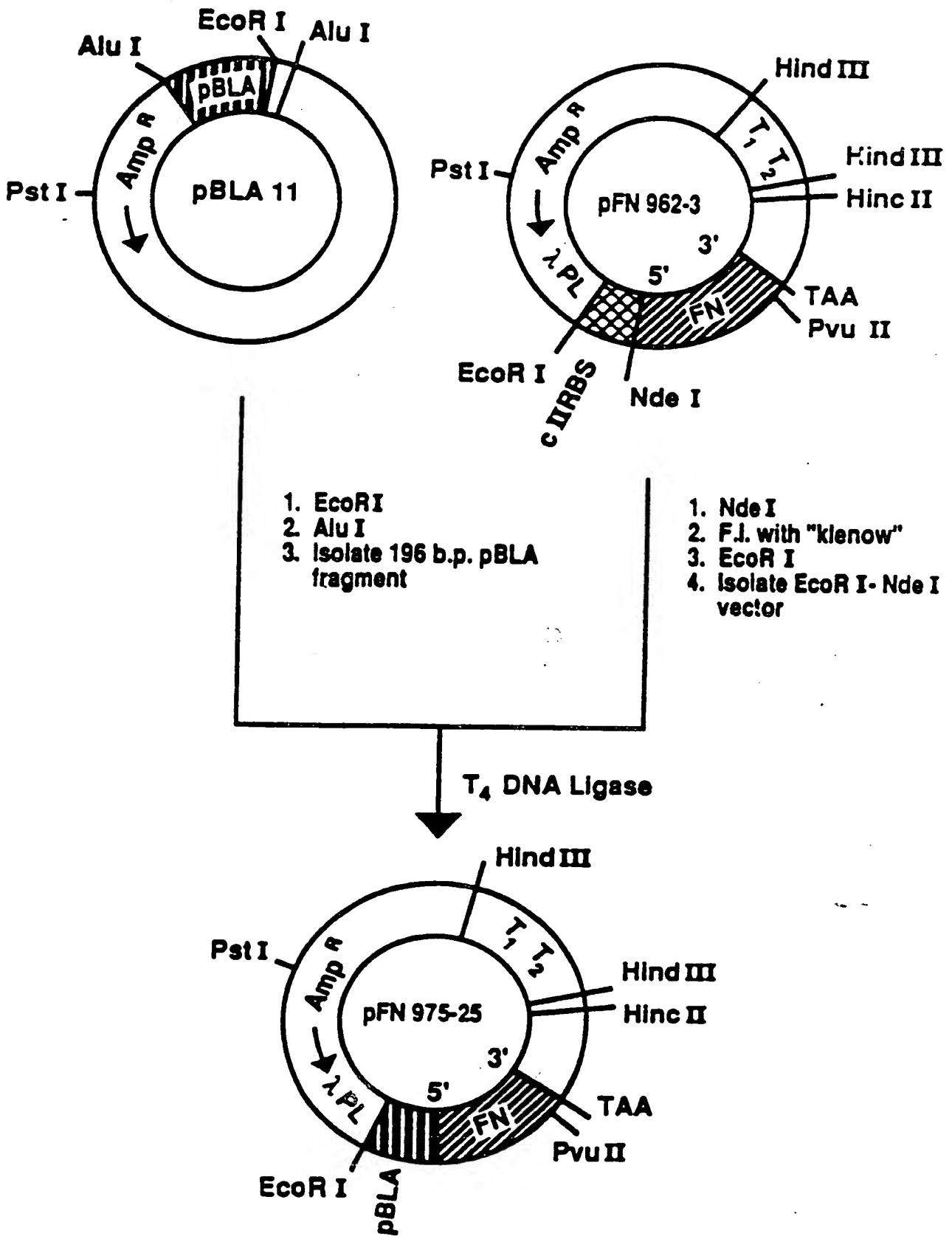


Figure 10



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Figure 11

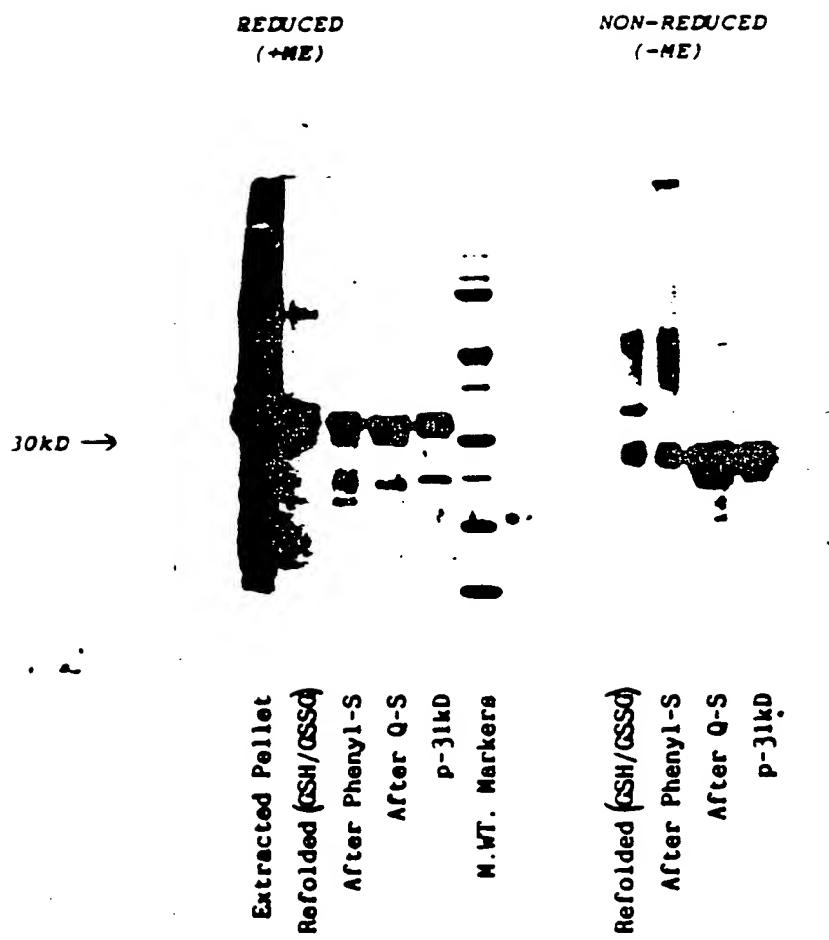
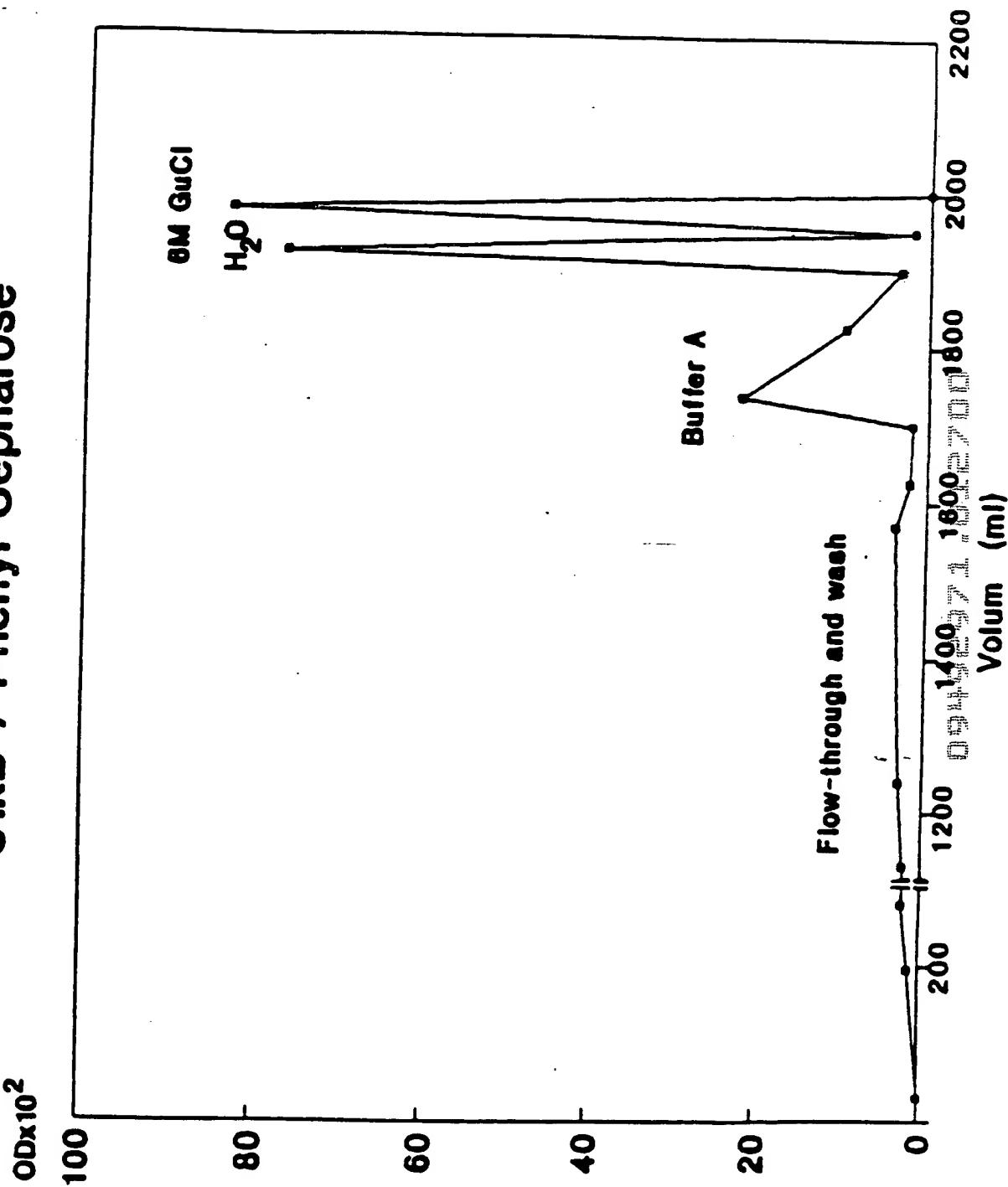
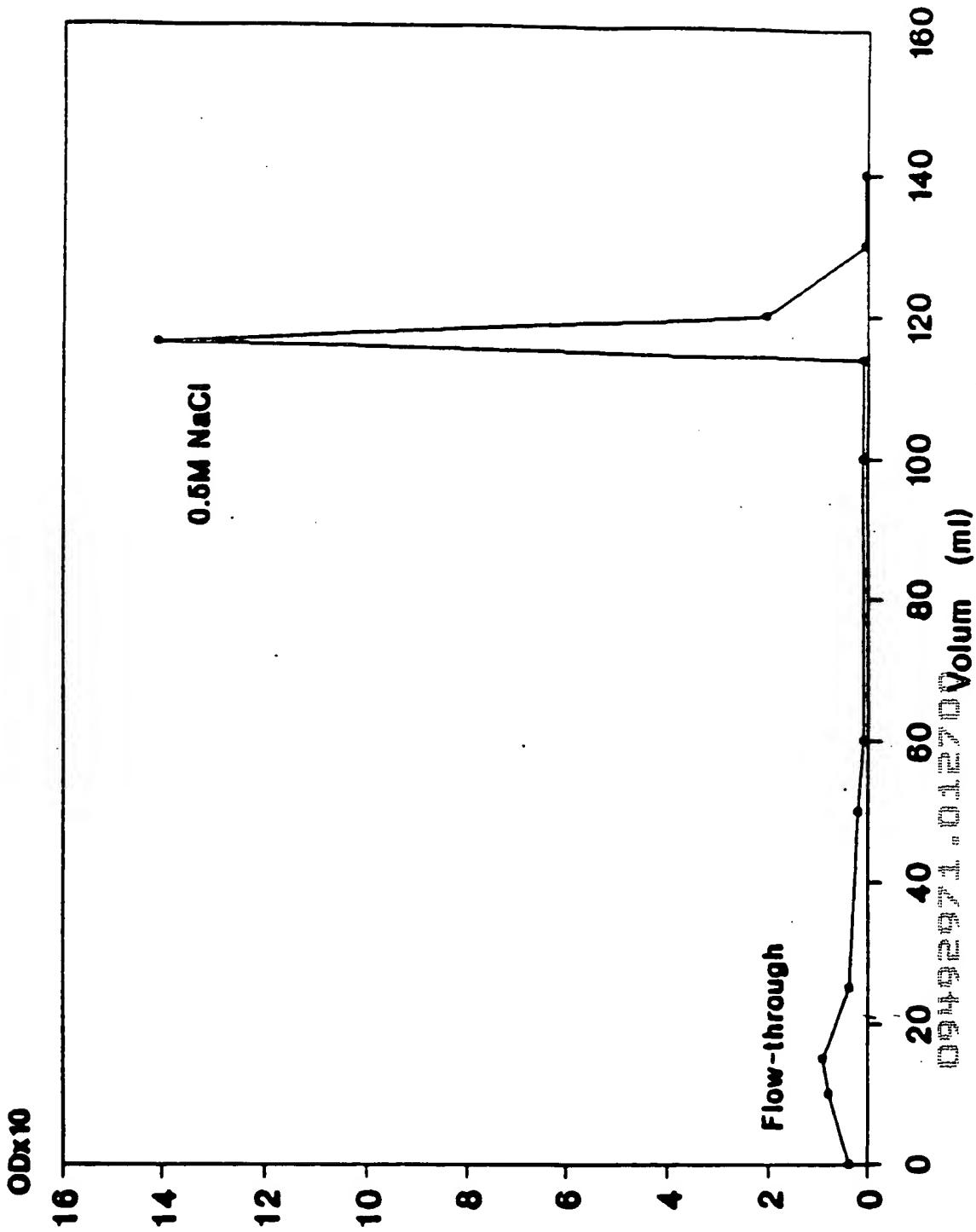


Figure 12
31kD / Phenyl-Sephadose



31kD/Heparin-Sephadex



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31kD / Q-Sephadose

Figure 14

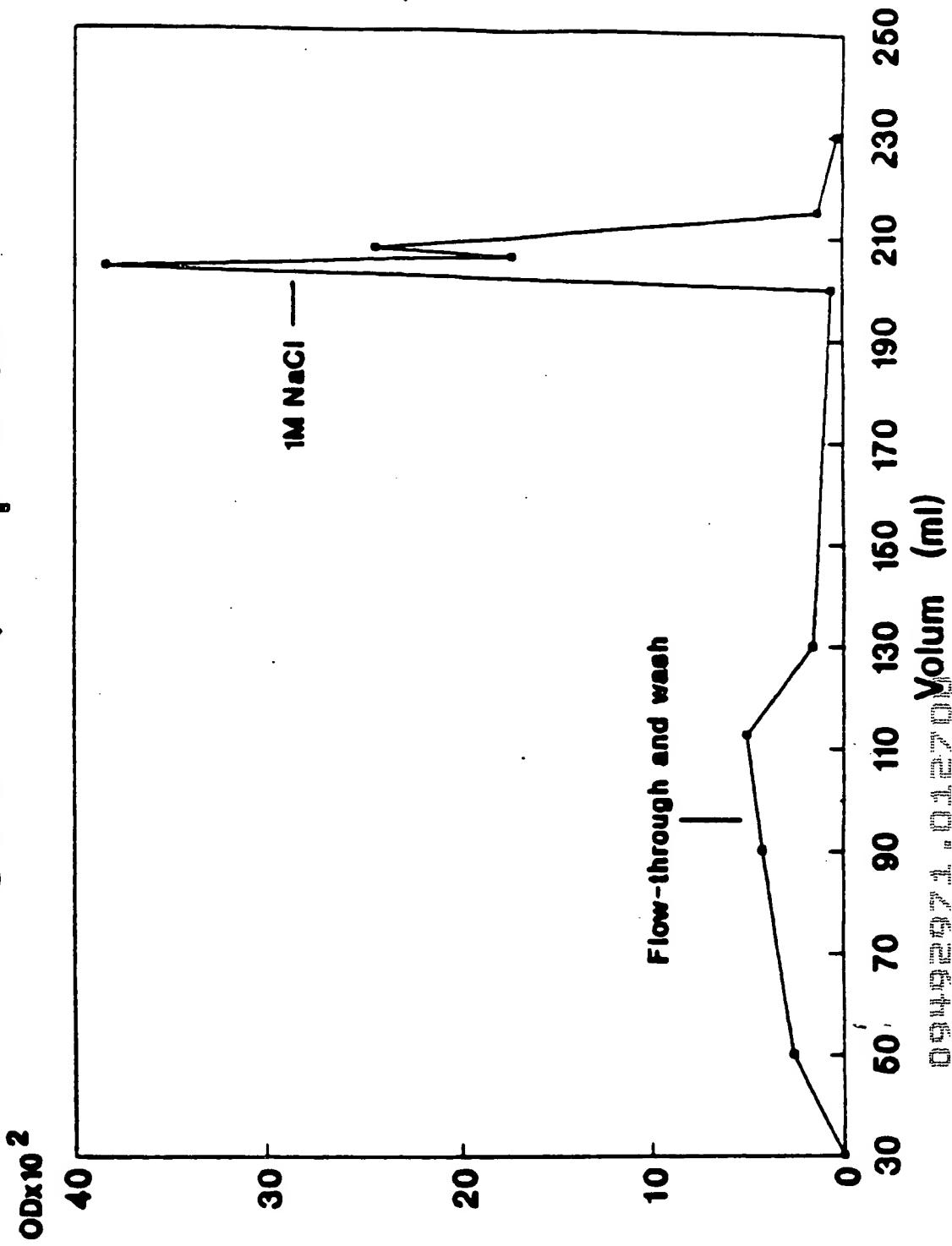
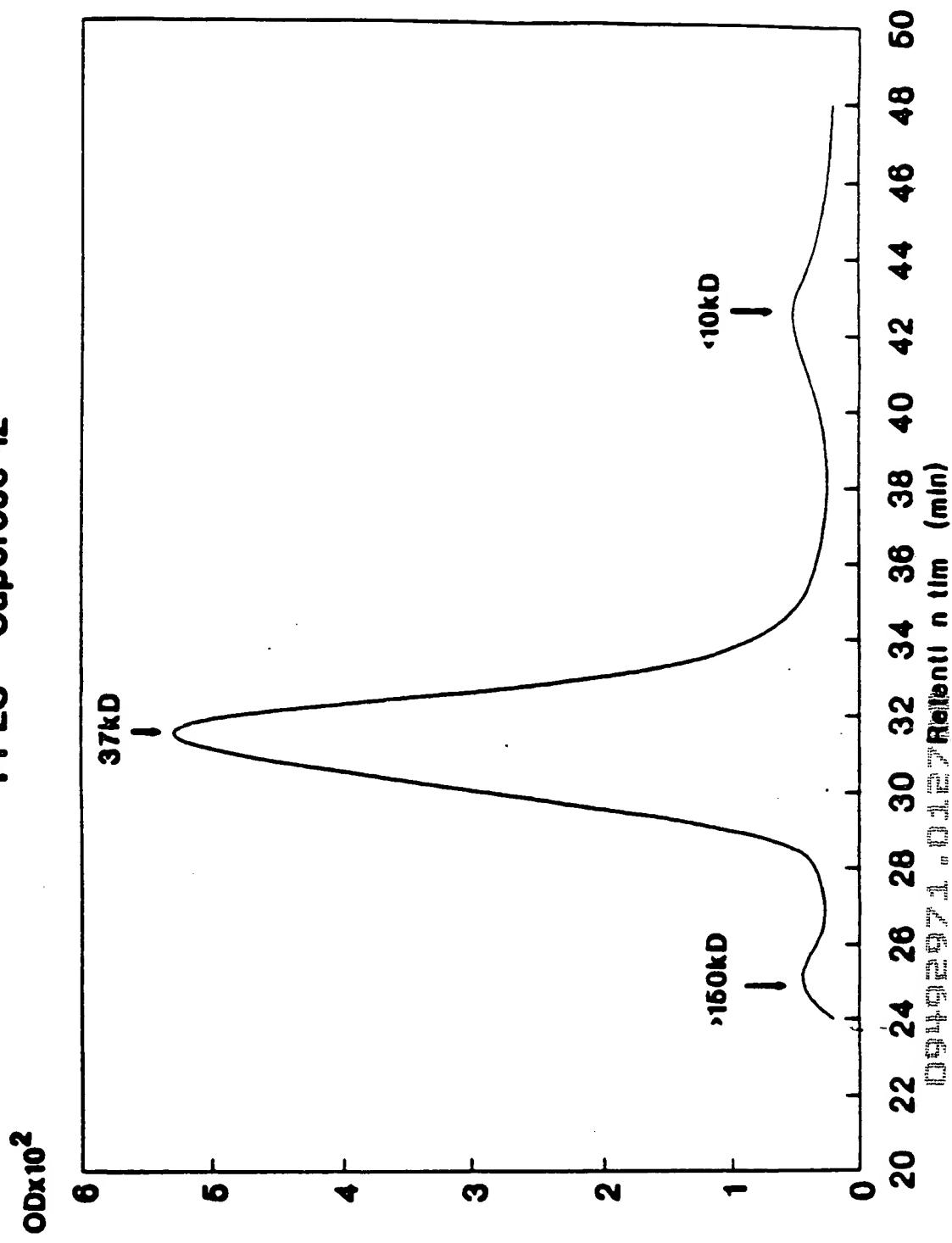


Figure 15
**Mixture of rec. and plasmatic "31kD" FBD
FPLC - Superose 12**



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Figure 16

Pharmacokinetic Behavior of Fibronectin
and Recombinant 31kD FBD in the Rat

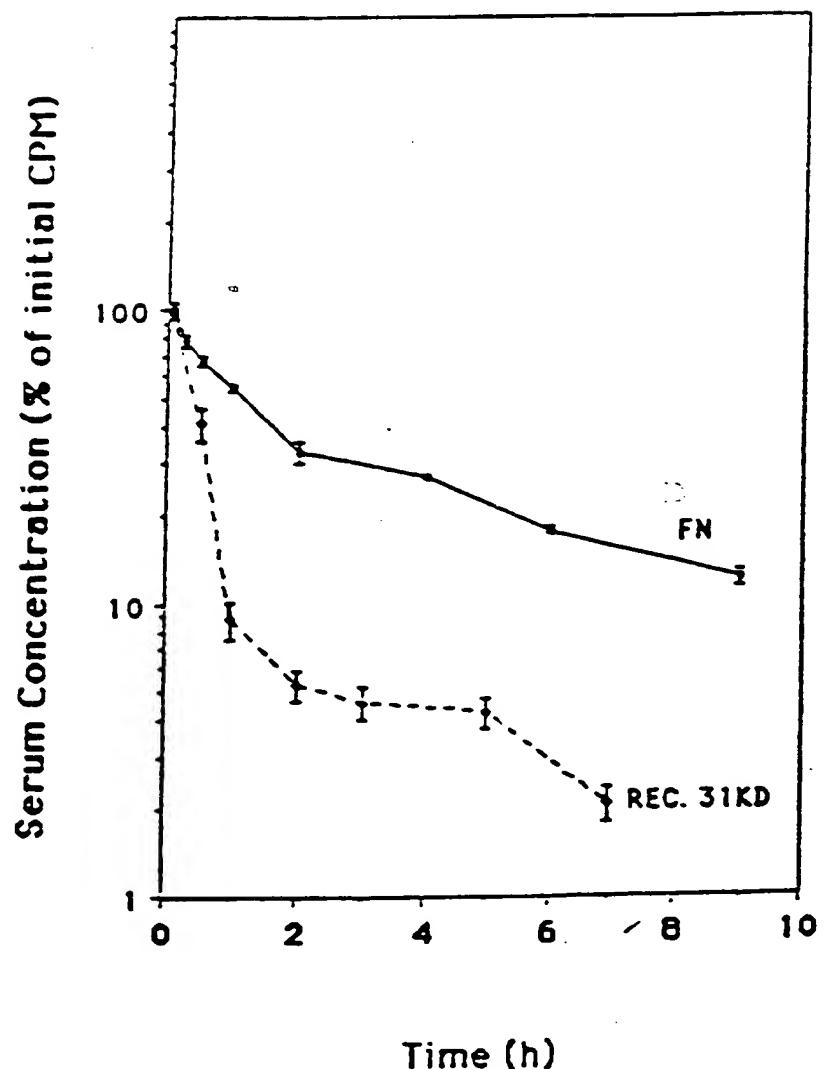
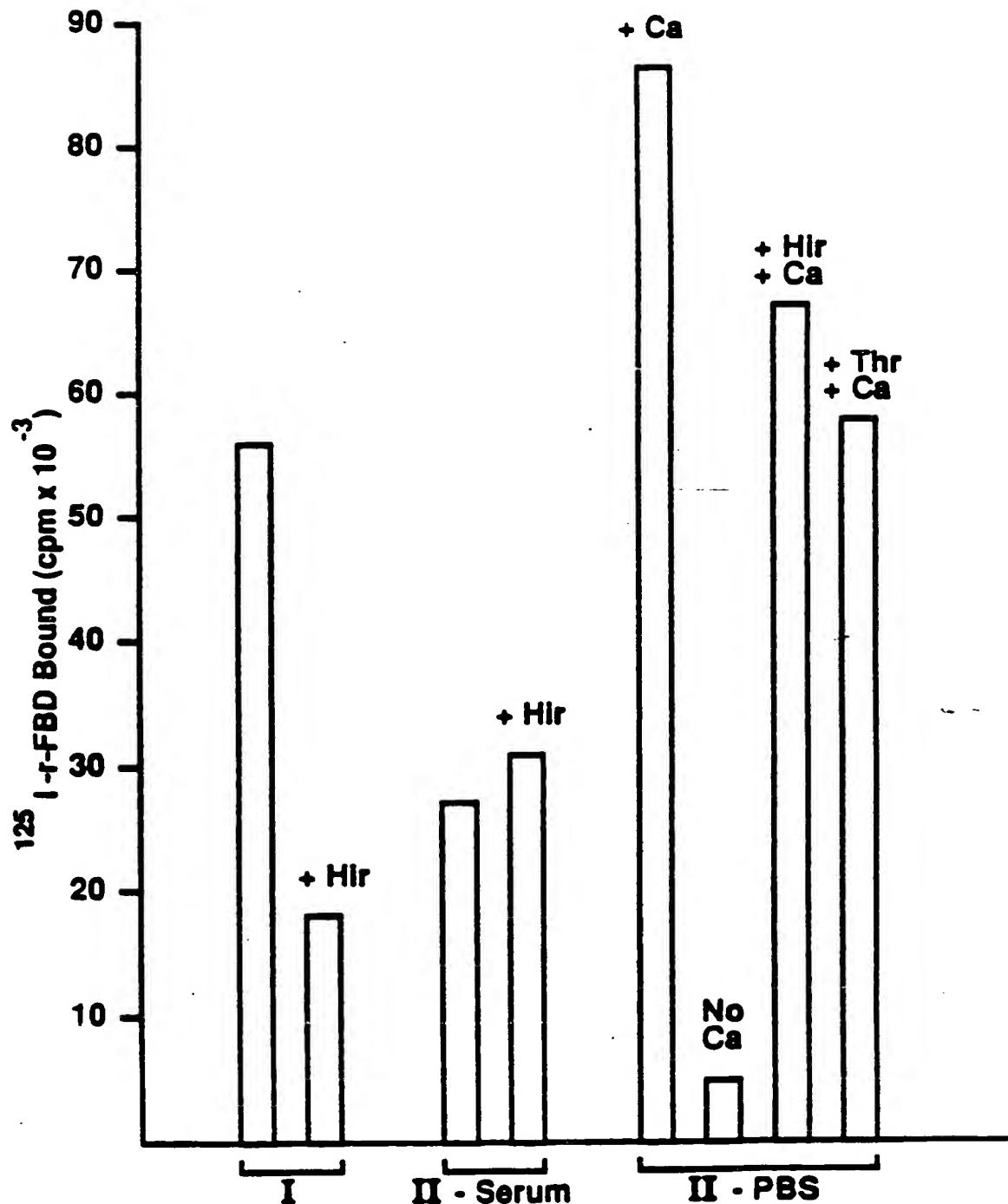


Figure 17

**Binding of ^{125}I -FBD to Fibrin;
Effect of Thrombin and Ca^{++} ions.**

I = Binding while clot formation
 II = Binding to preformed Fibrin clot



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Figure 18

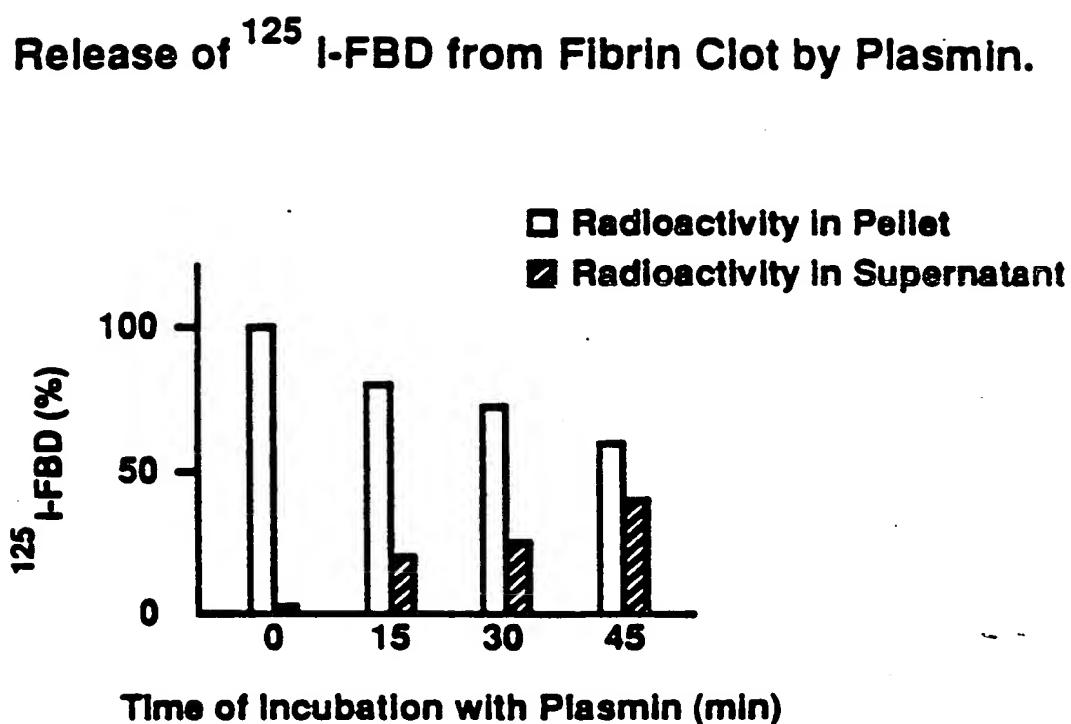


Figure 19

**Binding of ^{125}I -FBD during clot formation (Reaction I) ;
Effect of unlabelled FBD and related molecules.**

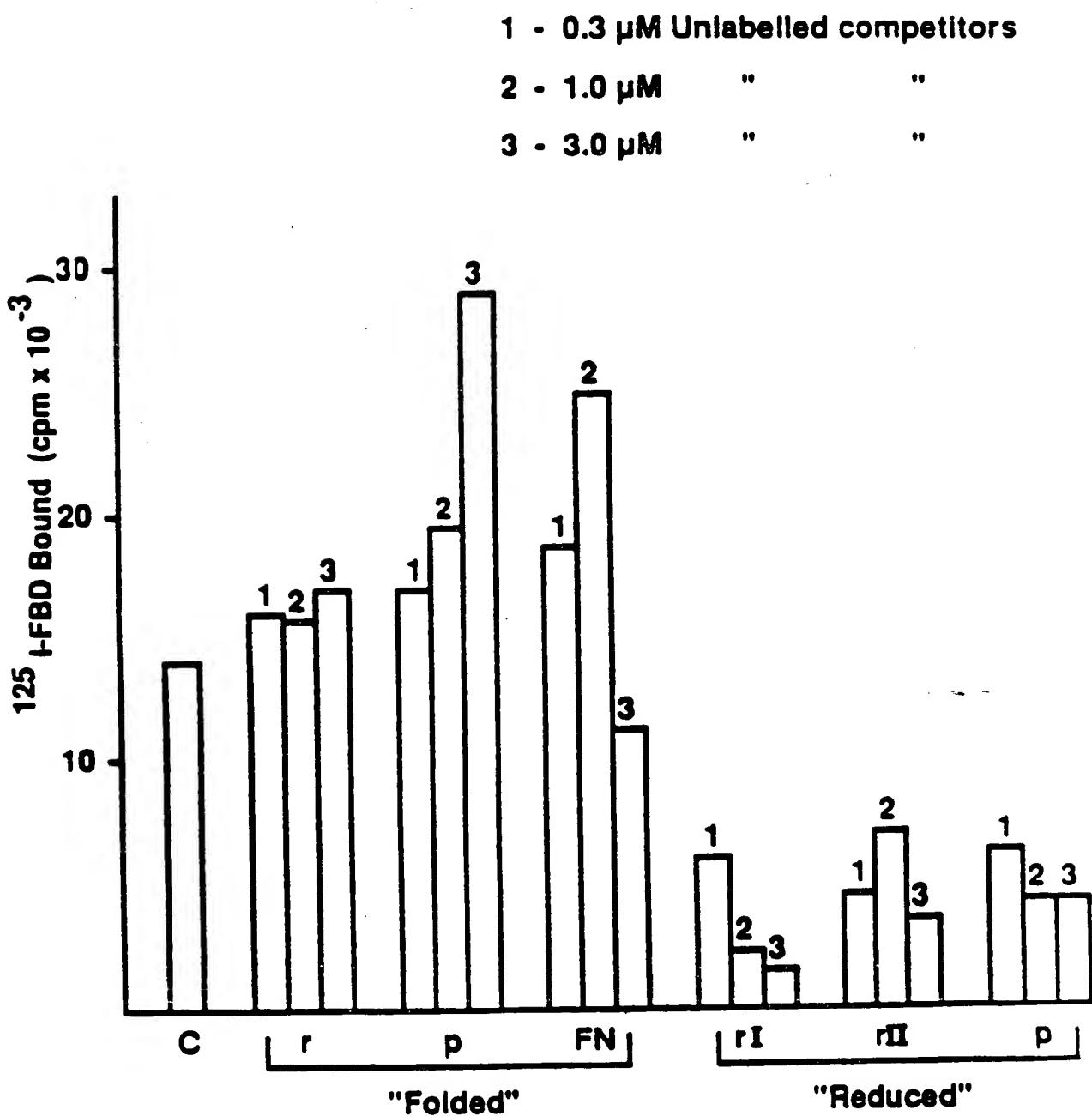


Figure 20

Binding of 125 I-FBD to Fibrin (Reaction II);
Effect of Transglutaminase Inhibitors.

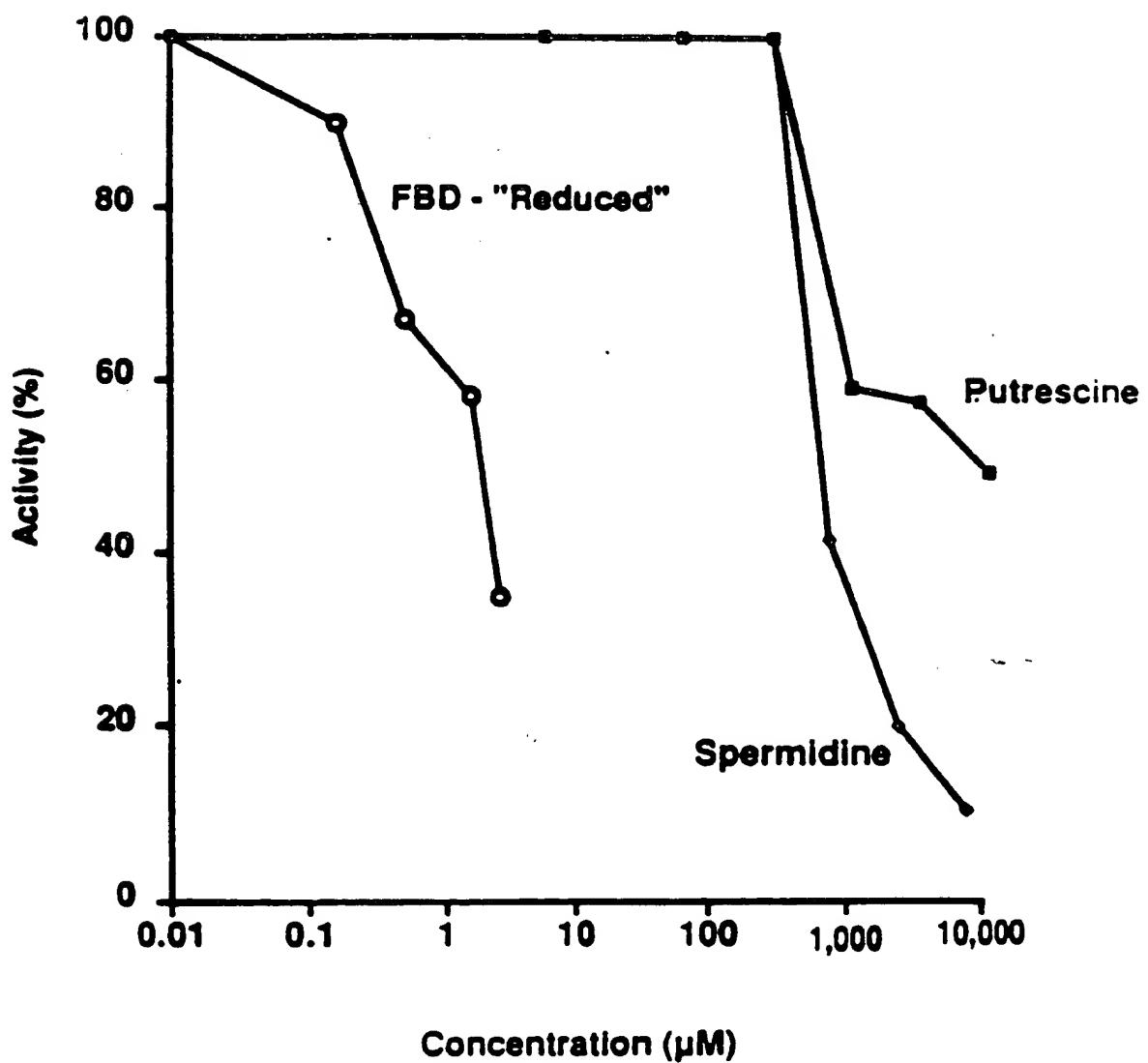


Figure 21

**Binding of ^{125}I -FBD to preformed Fibrin clot (Reaction II);
Effect of Fibrin clot Age on the Binding (aging at 37° C).**

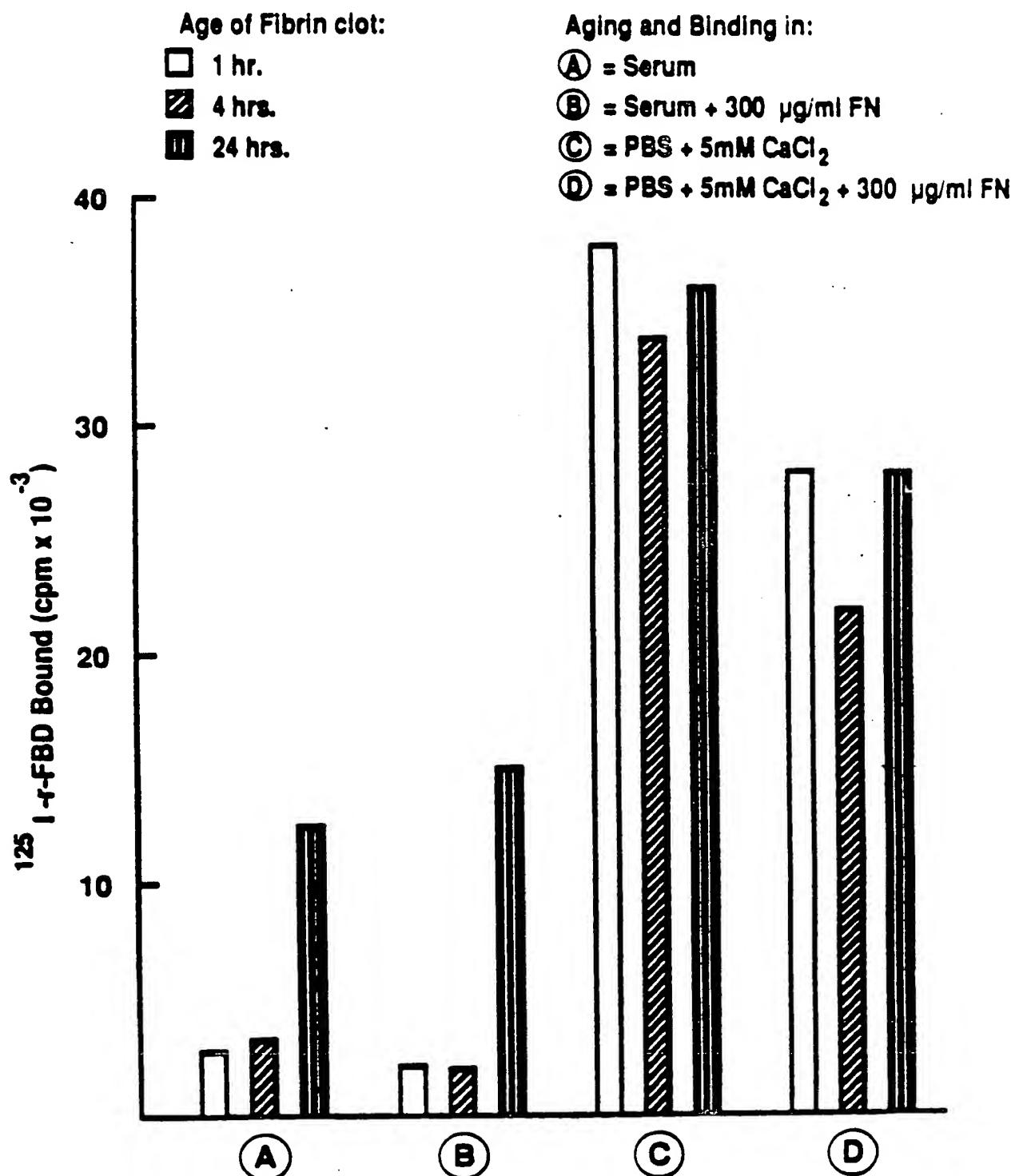


Figure 22

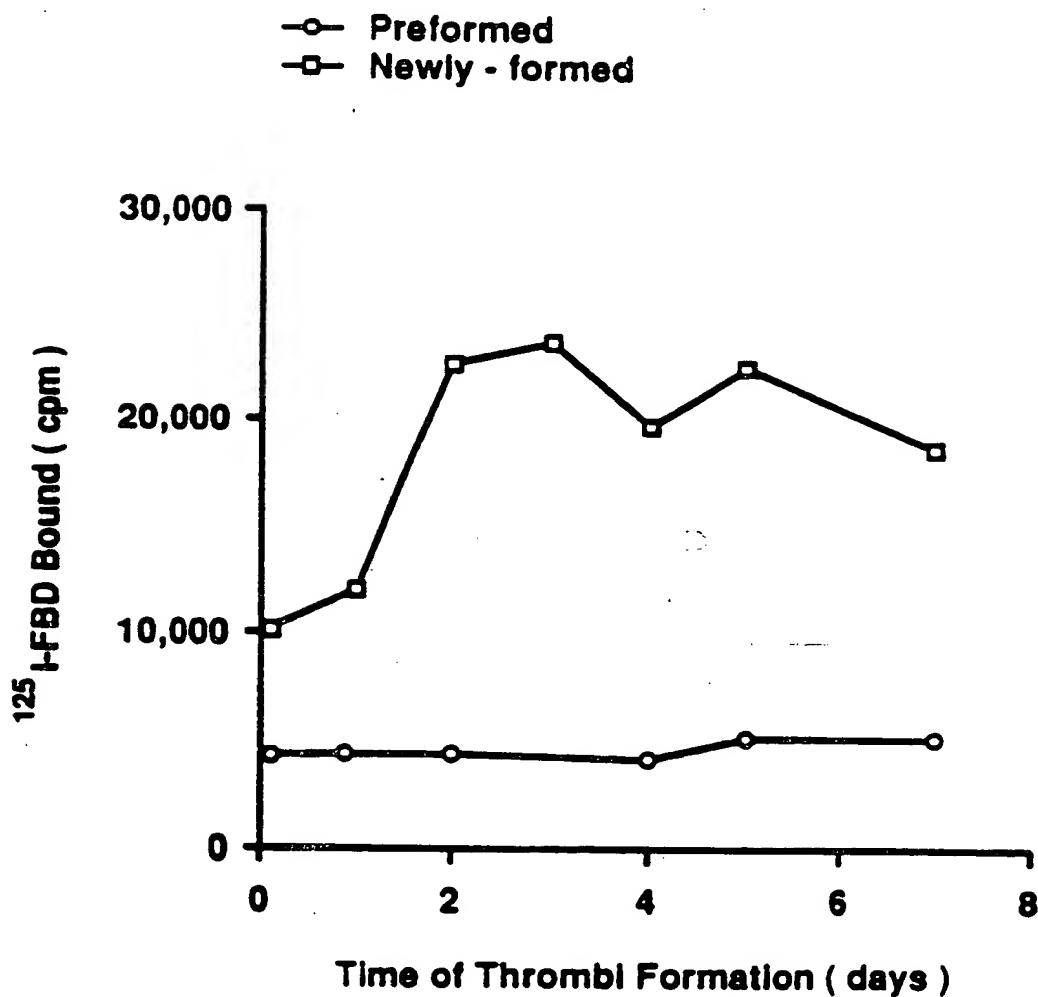
Binding of FBD to "Naive" Thrombi

Figure 23

**Binding of FBD to Fibrin (Reaction I);
Effect of Transglutaminase ("TG")
and "Reduced" - FBD**

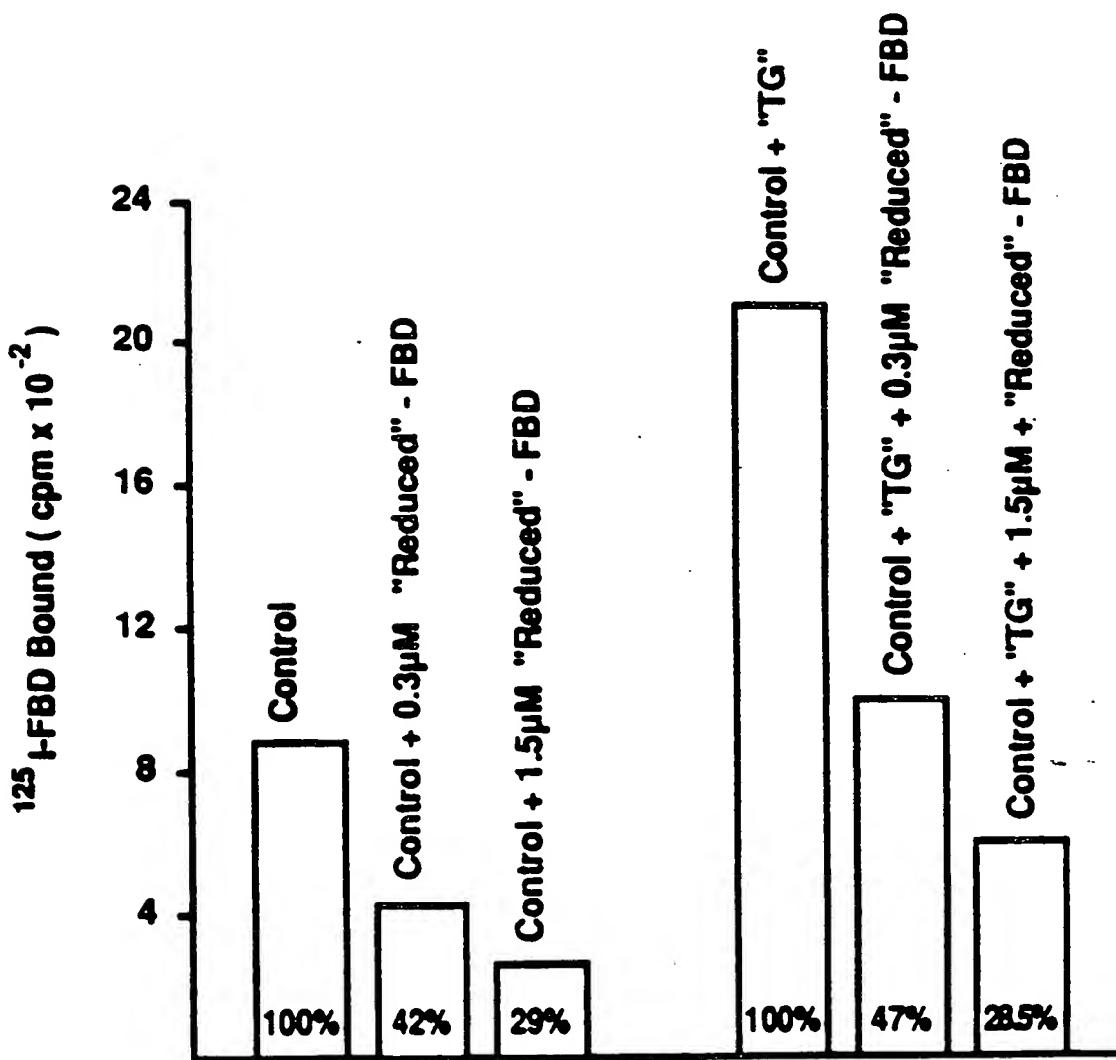


Figure 24

Binding of ^{125}I -FBD to ECM,
Effect of Ligand Concentration and Thrombin

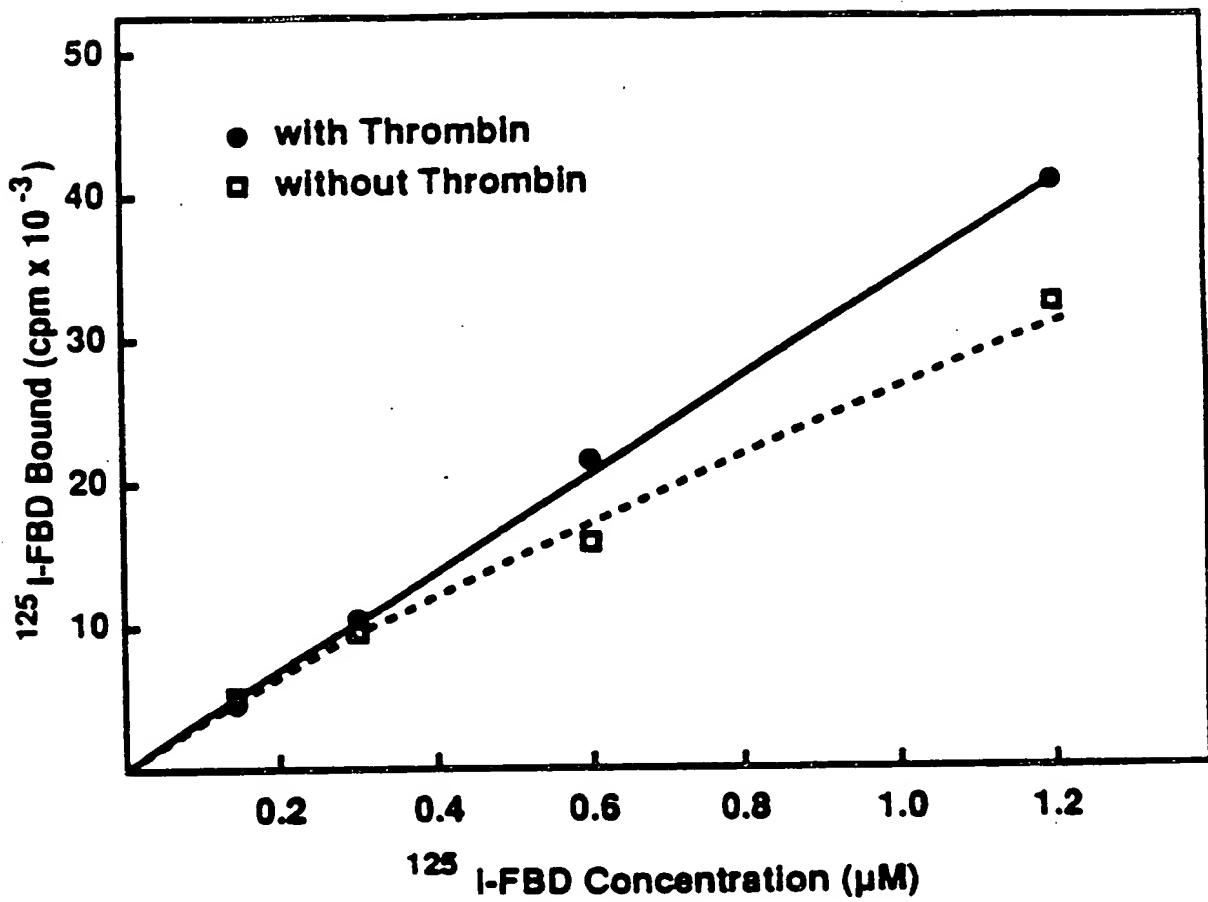


Figure 25

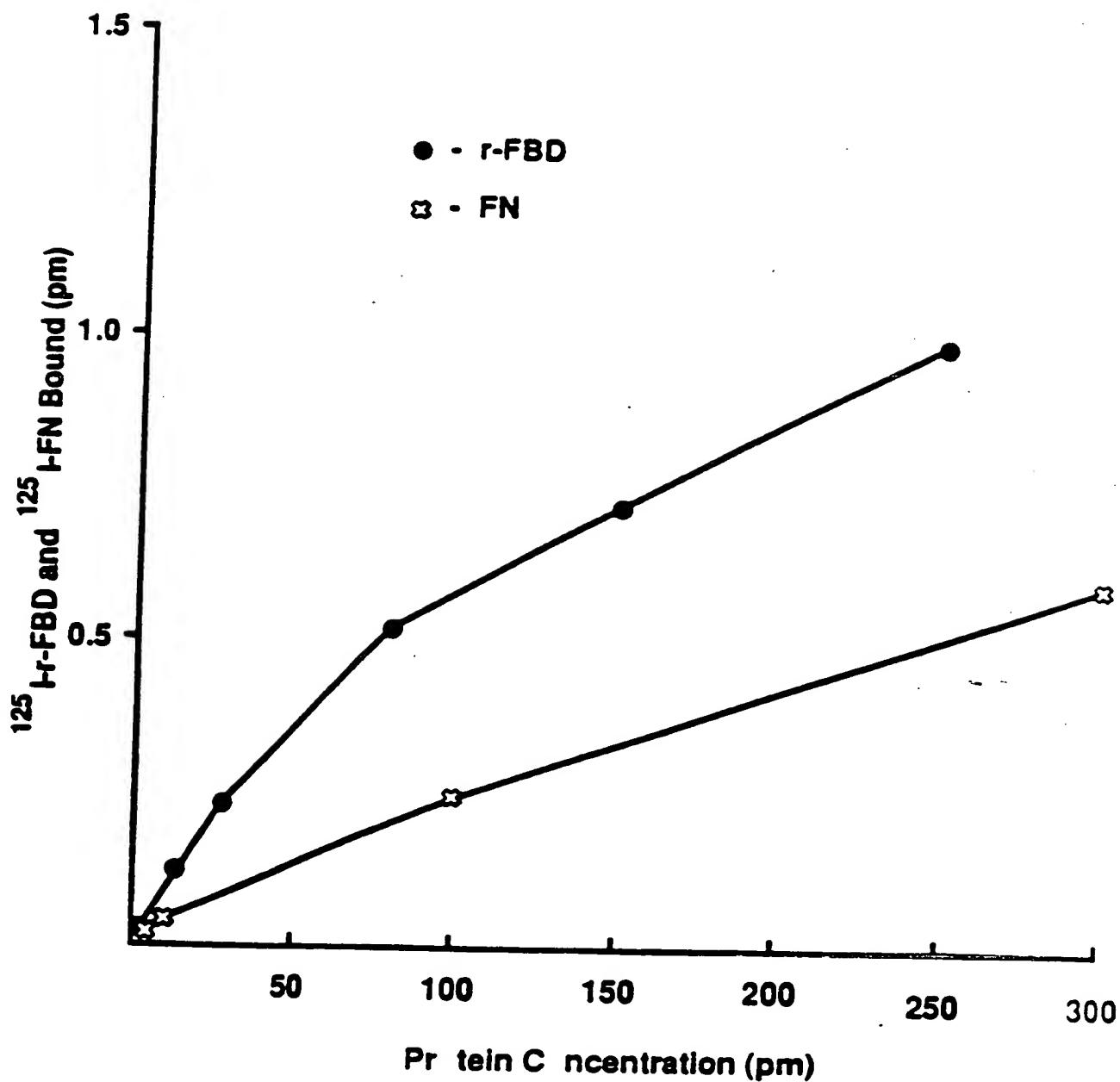
Binding of ^{125}I - (FN, r-FBD) to S. aureus

Figure 26

Binding of ^{125}I -FBD to *S. aureus*;
Competition with "Folded" and "Reduced" forms.

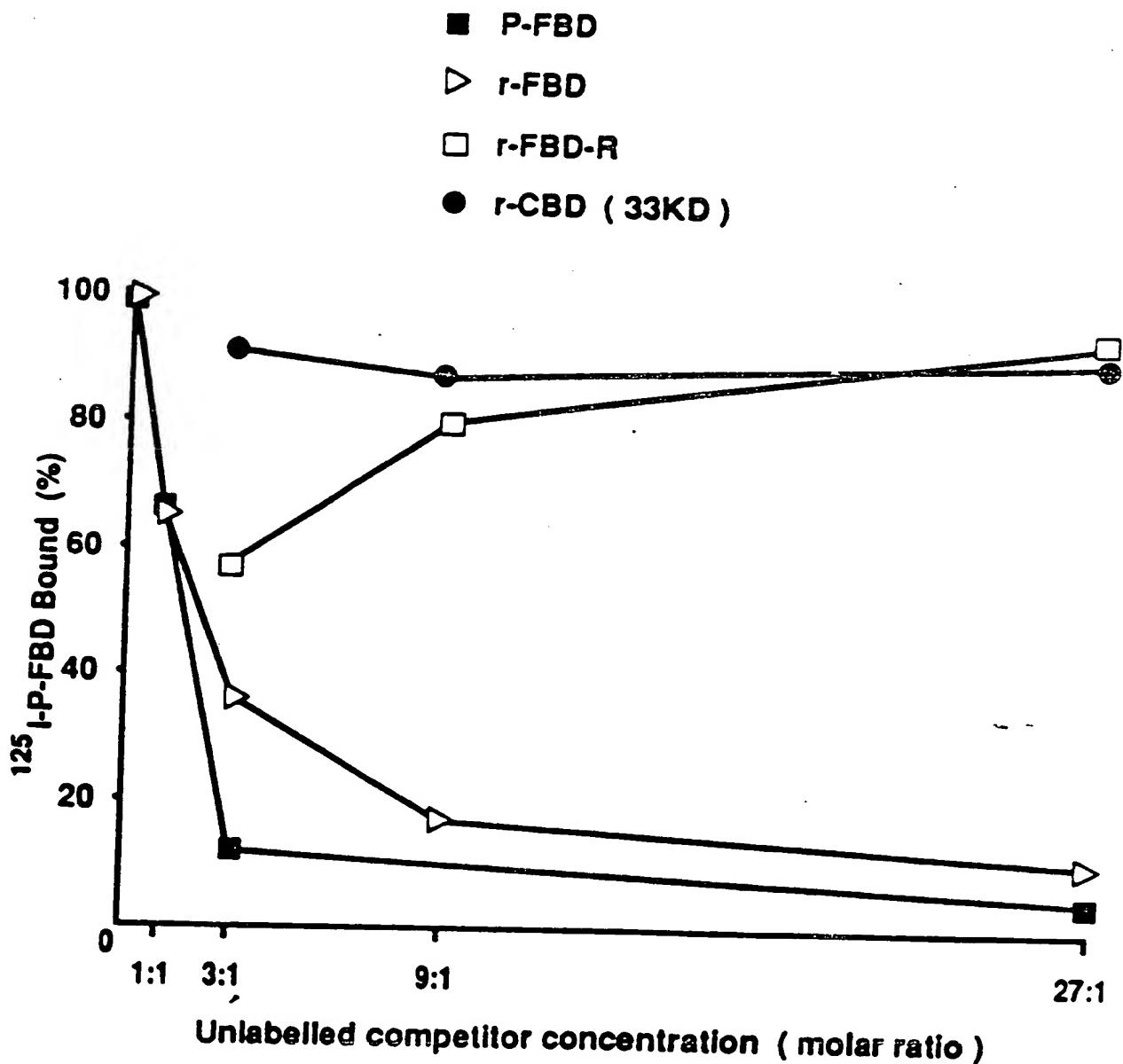


Figure 27

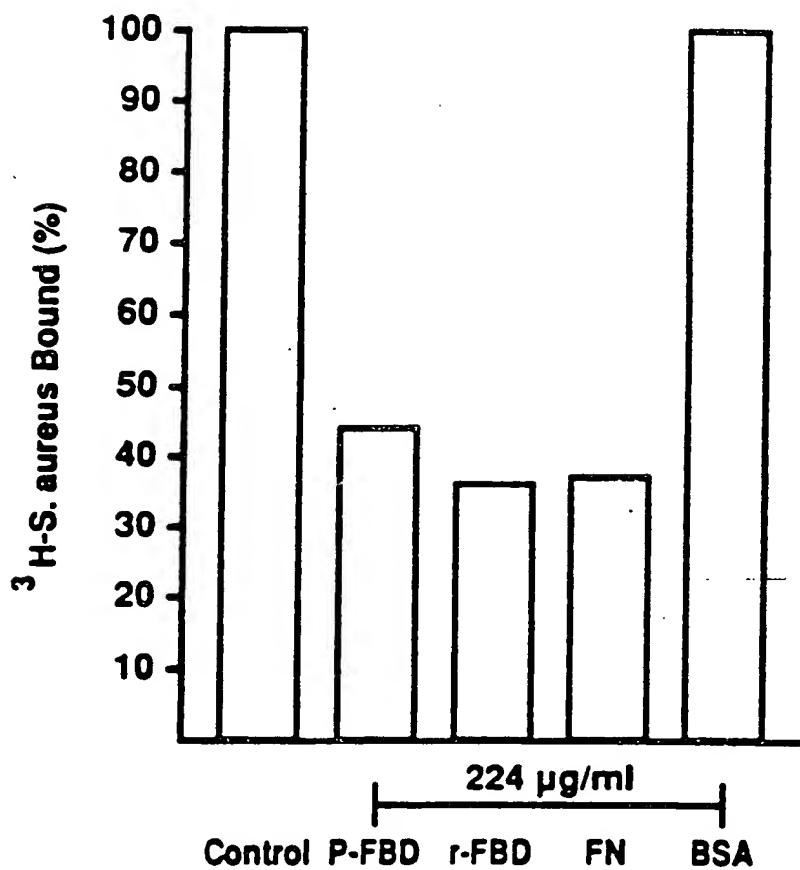
Binding of S. aureus to Immobilized FN.

Figure 28

**Binding of *S. aureus* to Bronchial Catheters;
Effect of FBD and Heparin.**

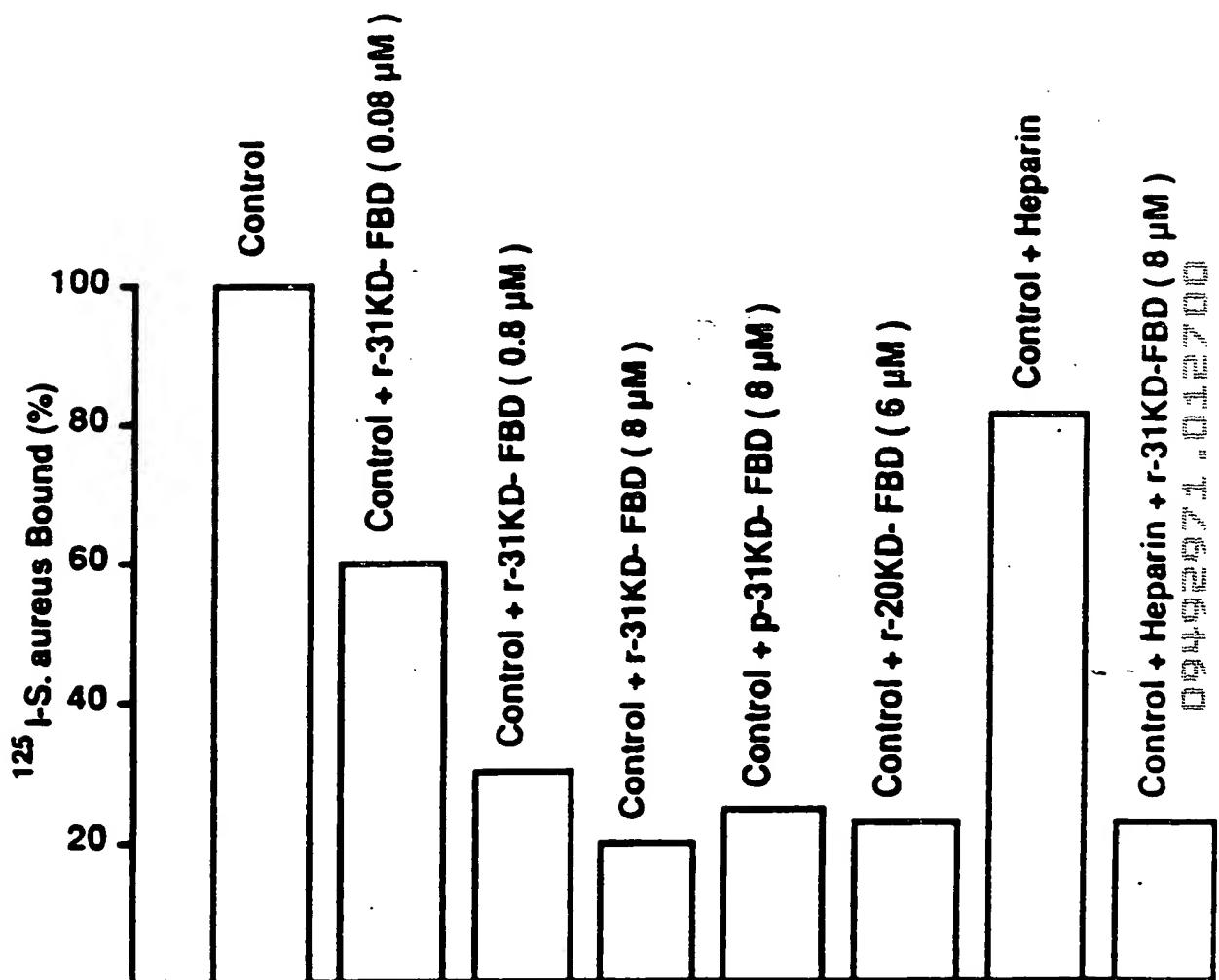


Figure 29A

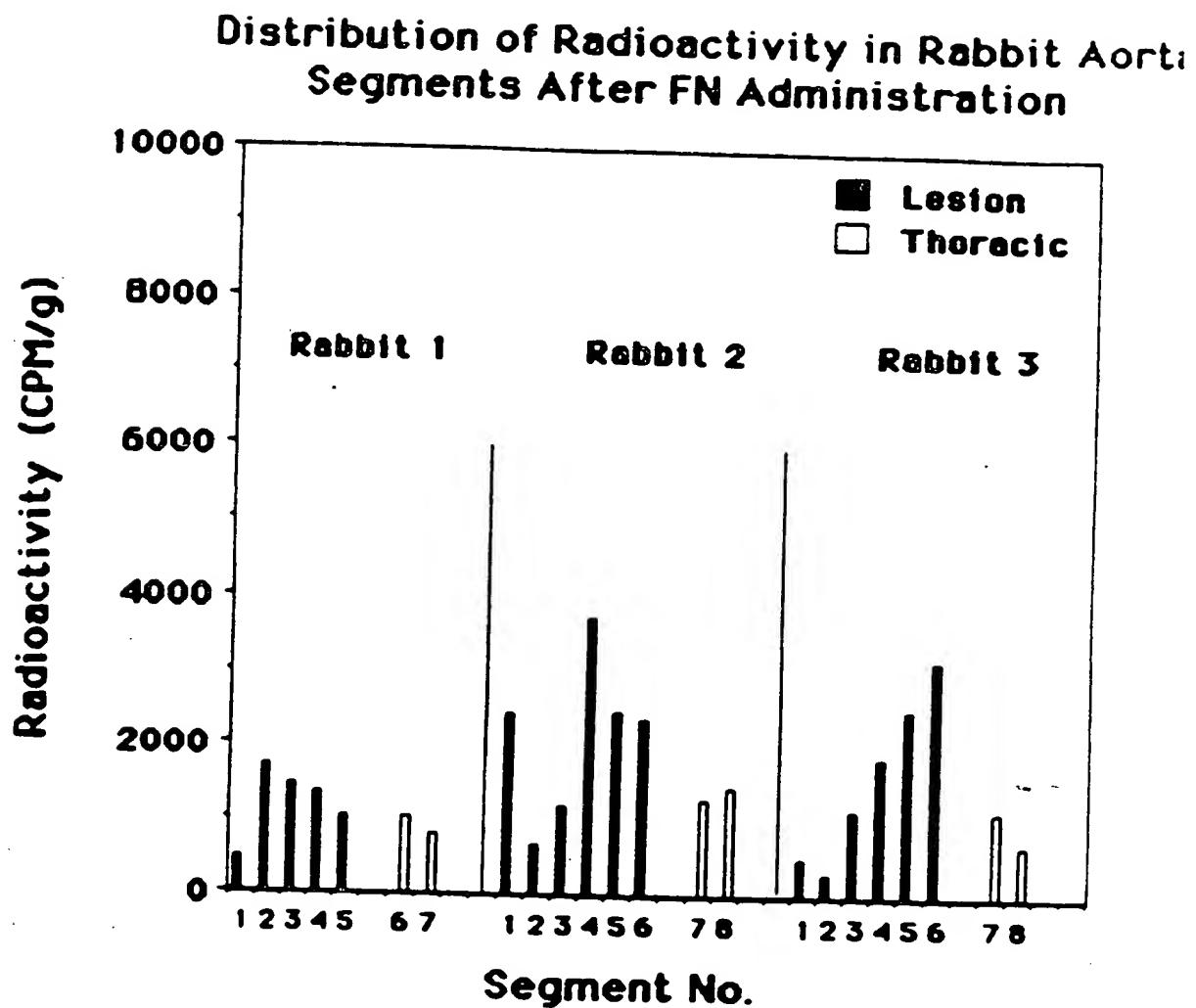


Figure 29B

Distribution of Radioactivity in Rabbit Aorta Segments After 31kD FBD Administration

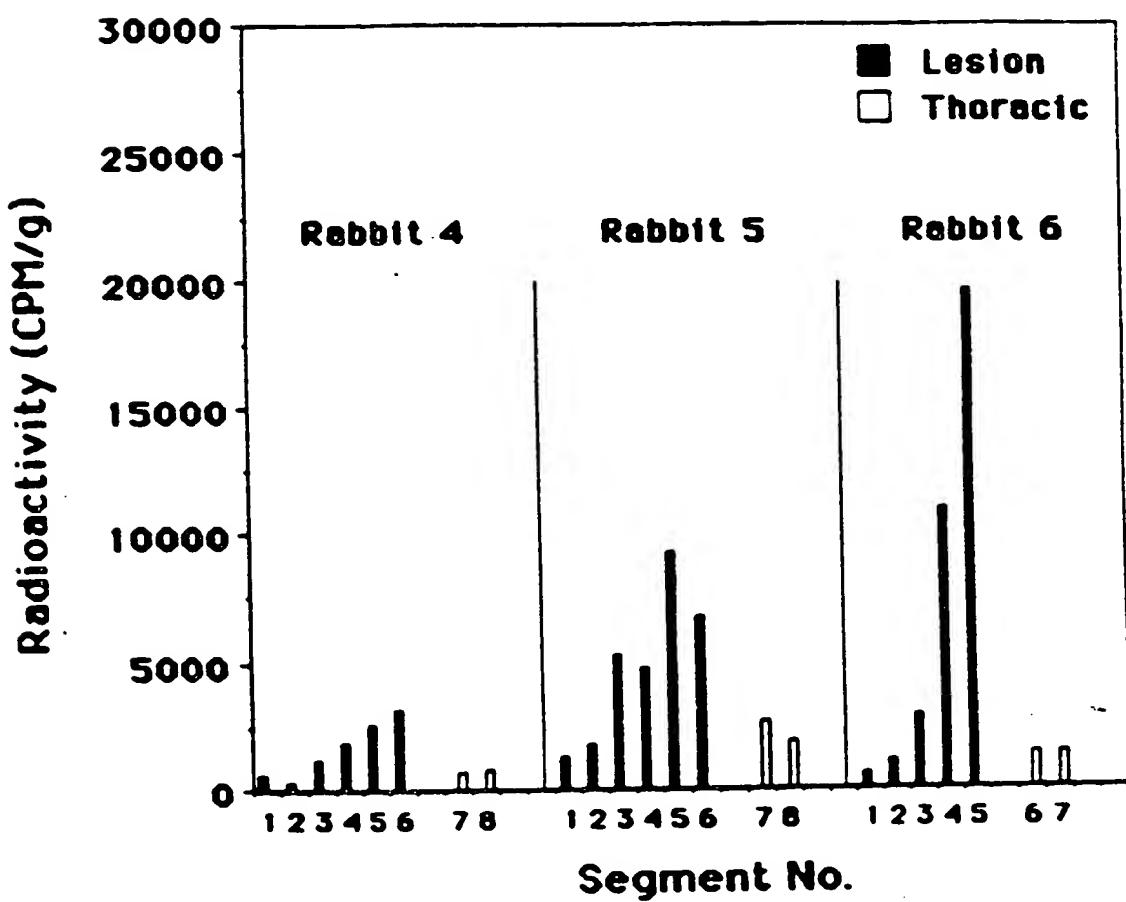


Figure 30

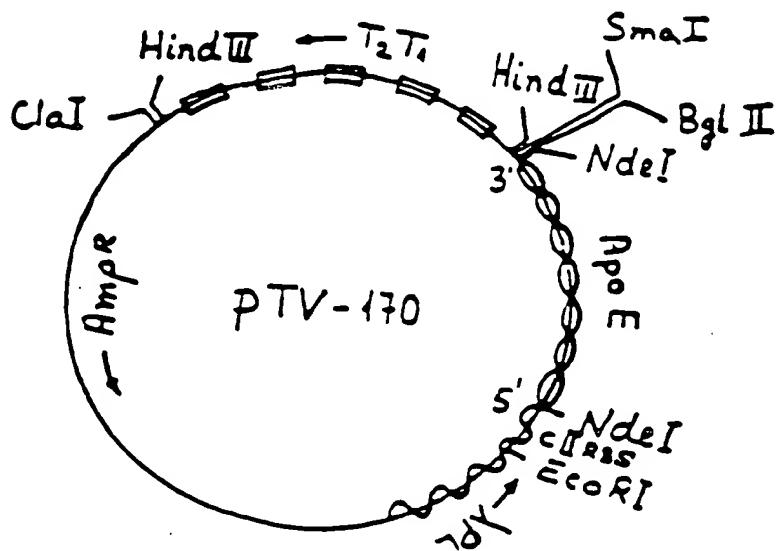
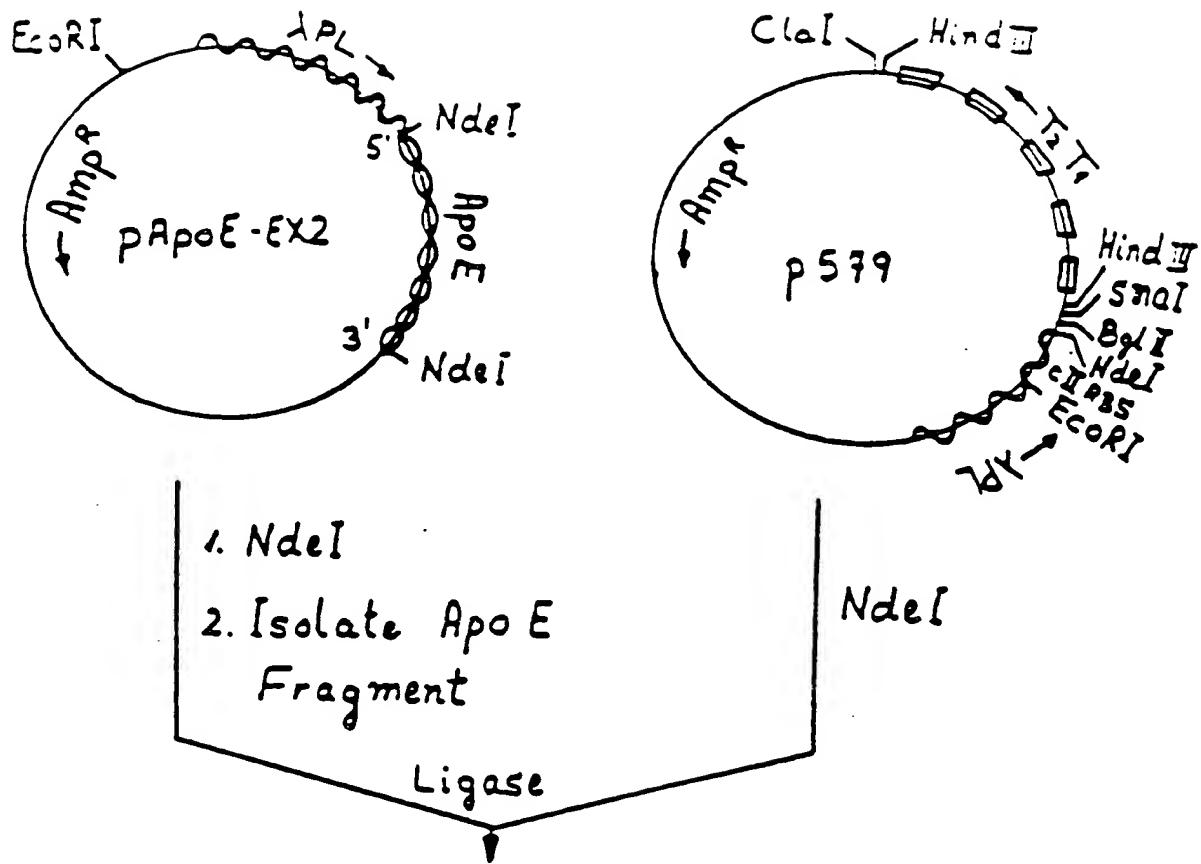
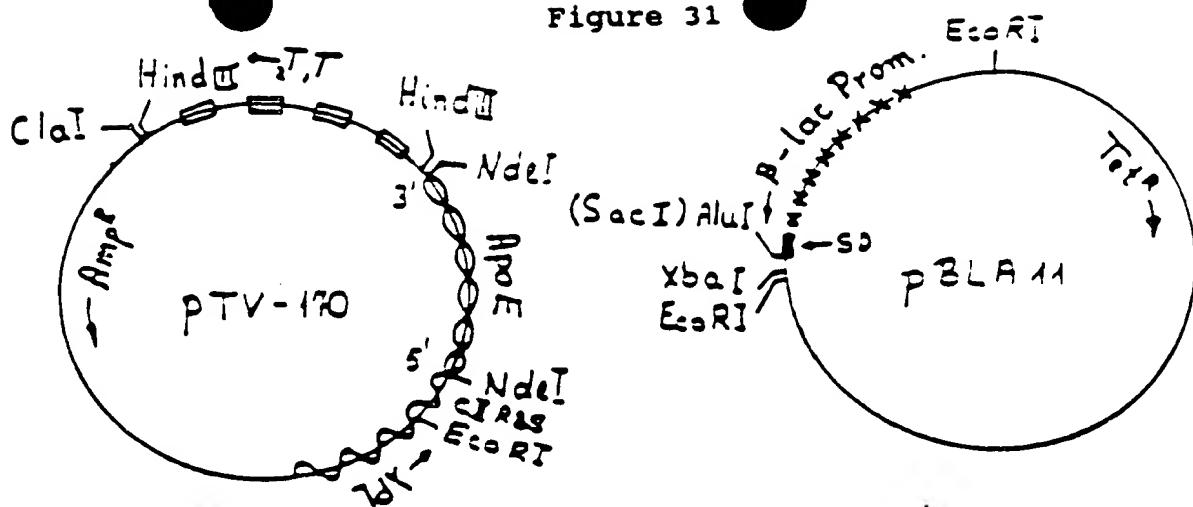
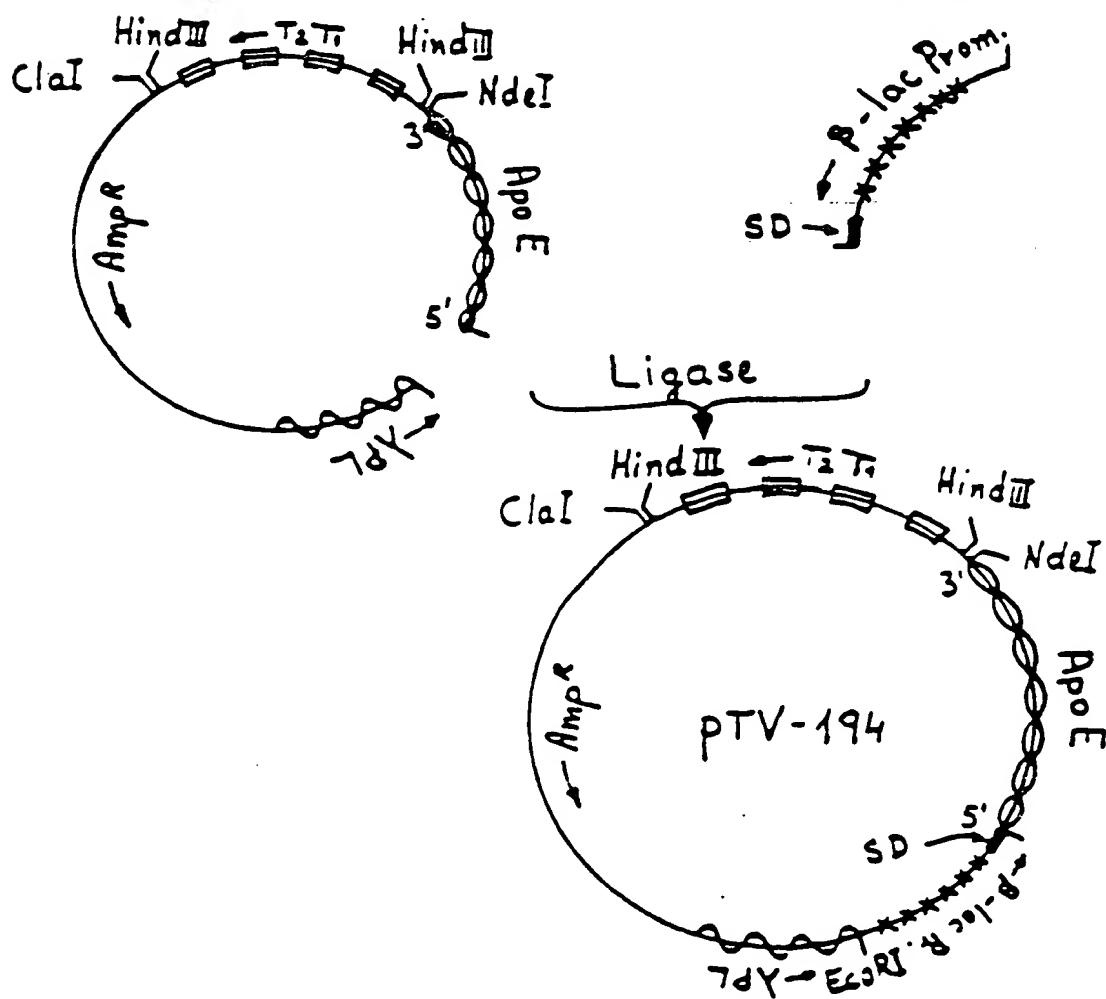


Figure 31



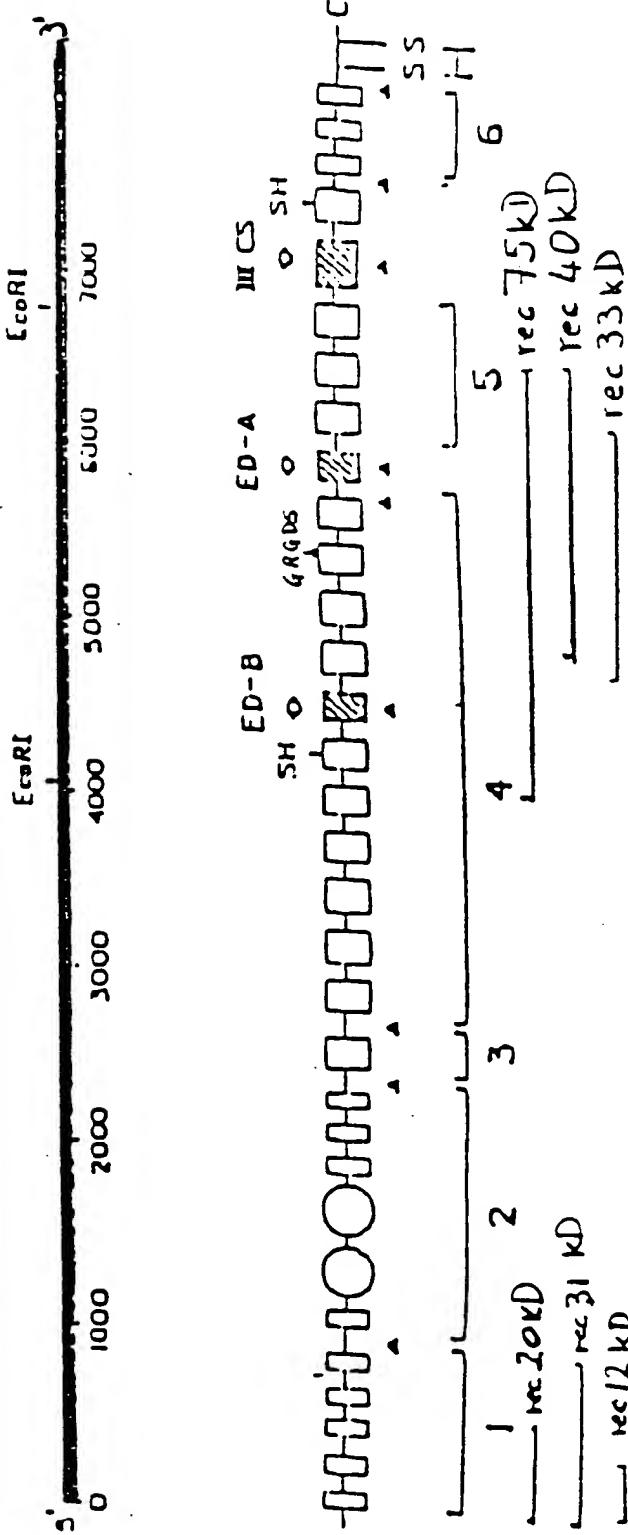
1. Partial *Nde*I
2. Fill in
3. *Eco*RI
4. Isolate Large Fragment

1. *Alu*I + *Eco*RI
2. Isolate 2008 bp Fragment



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Figur 32



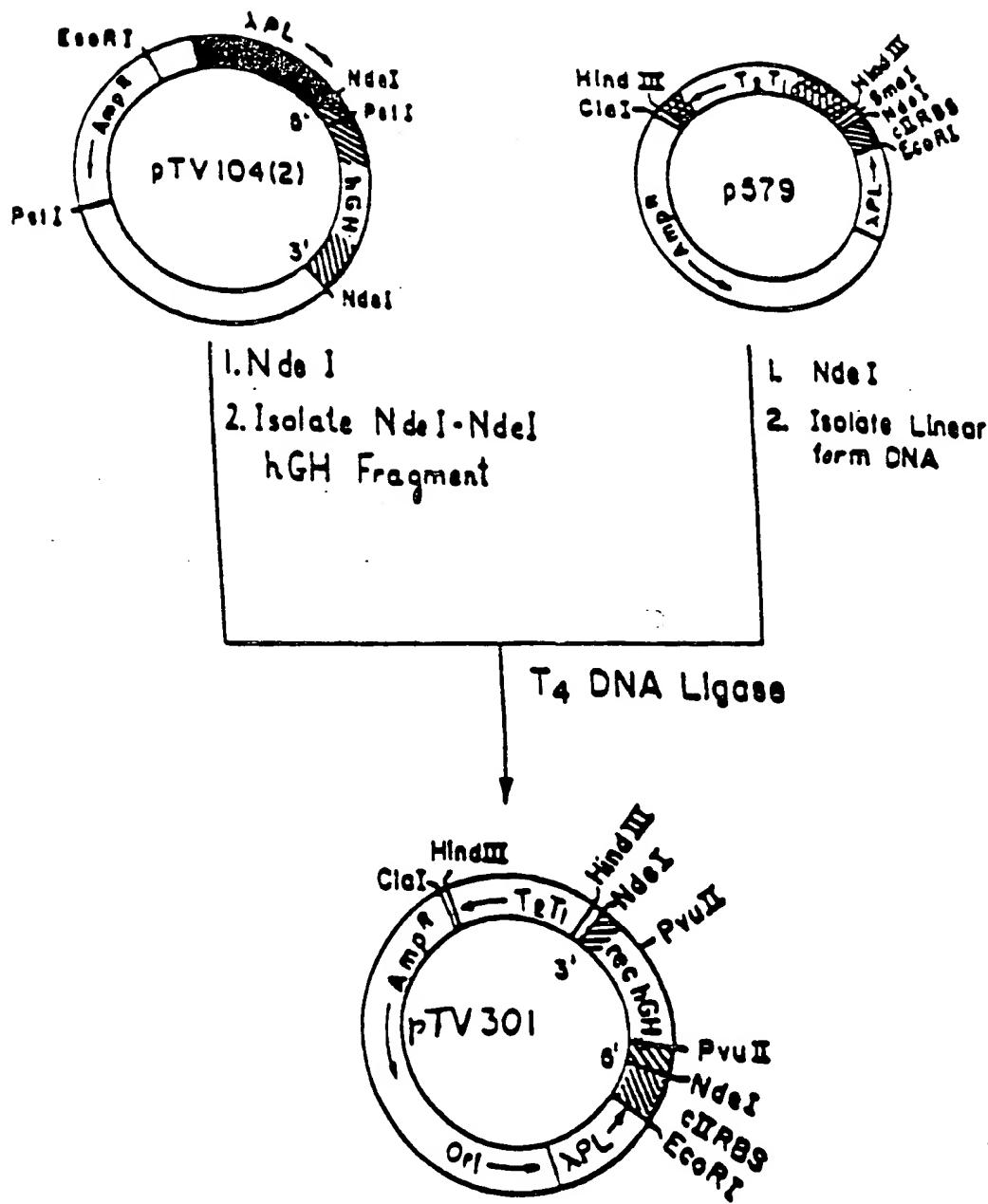
| | | | | |
|-----------|----------|---|------|---------|
| HEPARIN | COLLAGEN | $\left[\begin{matrix} \text{HEPARIN} \\ \text{DNA} \end{matrix} \right]$ | CELL | HEPARIN |
| S. AUREUS | | | | |
| FIBRIN | | | | |

Nucleotides

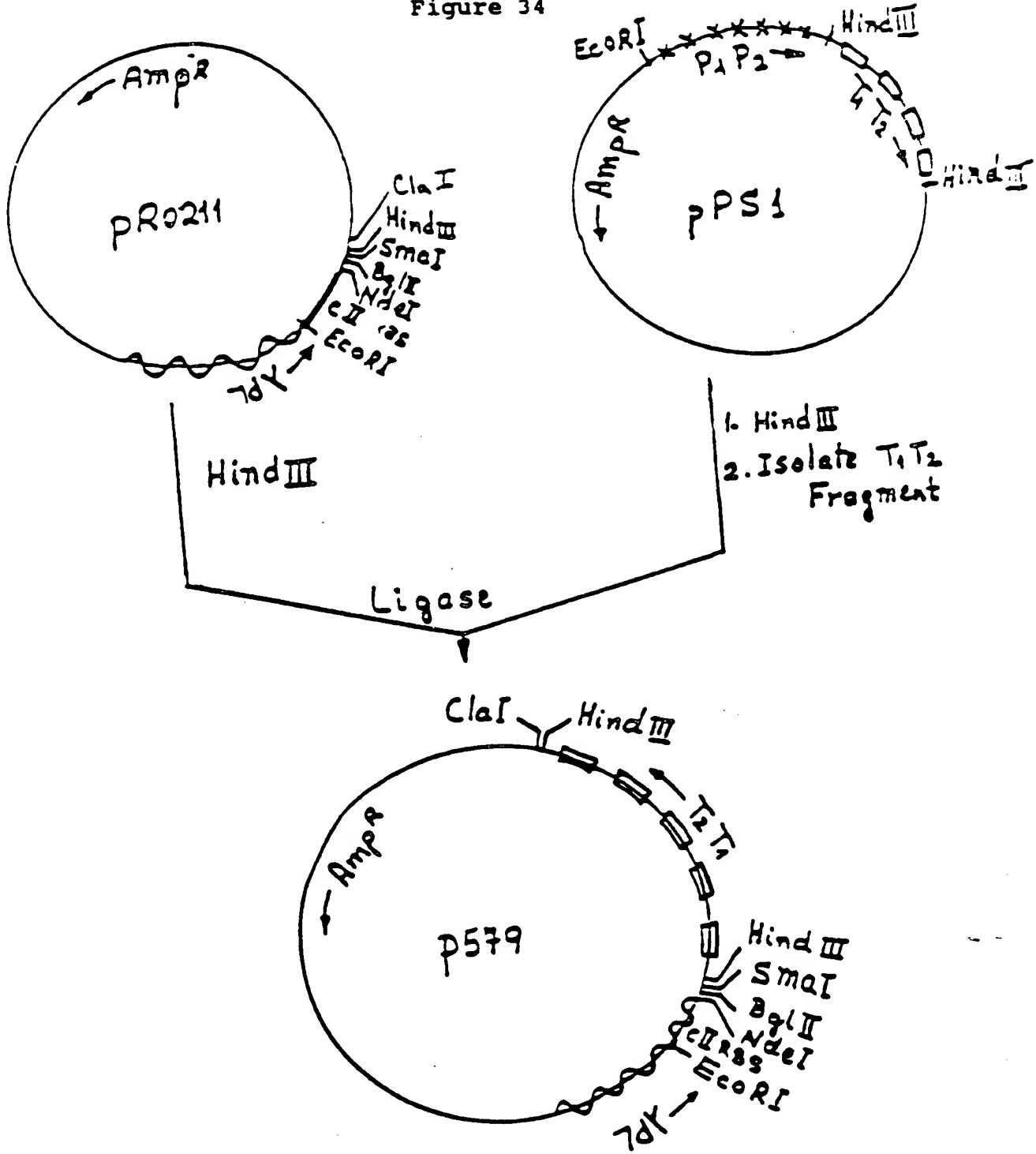
| | | | |
|------------|------------------|------------------|------------------|
| FBD | $\Sigma F_x = 0$ | $\Sigma M_x = 0$ | $\Sigma F_y = 0$ |
| | $\Sigma F_x = 0$ | $\Sigma M_x = 0$ | $\Sigma F_y = 0$ |
| | $\Sigma F_x = 0$ | $\Sigma M_x = 0$ | $\Sigma F_y = 0$ |
| | $\Sigma F_x = 0$ | $\Sigma M_x = 0$ | $\Sigma F_y = 0$ |
| | $\Sigma F_x = 0$ | $\Sigma M_x = 0$ | $\Sigma F_y = 0$ |

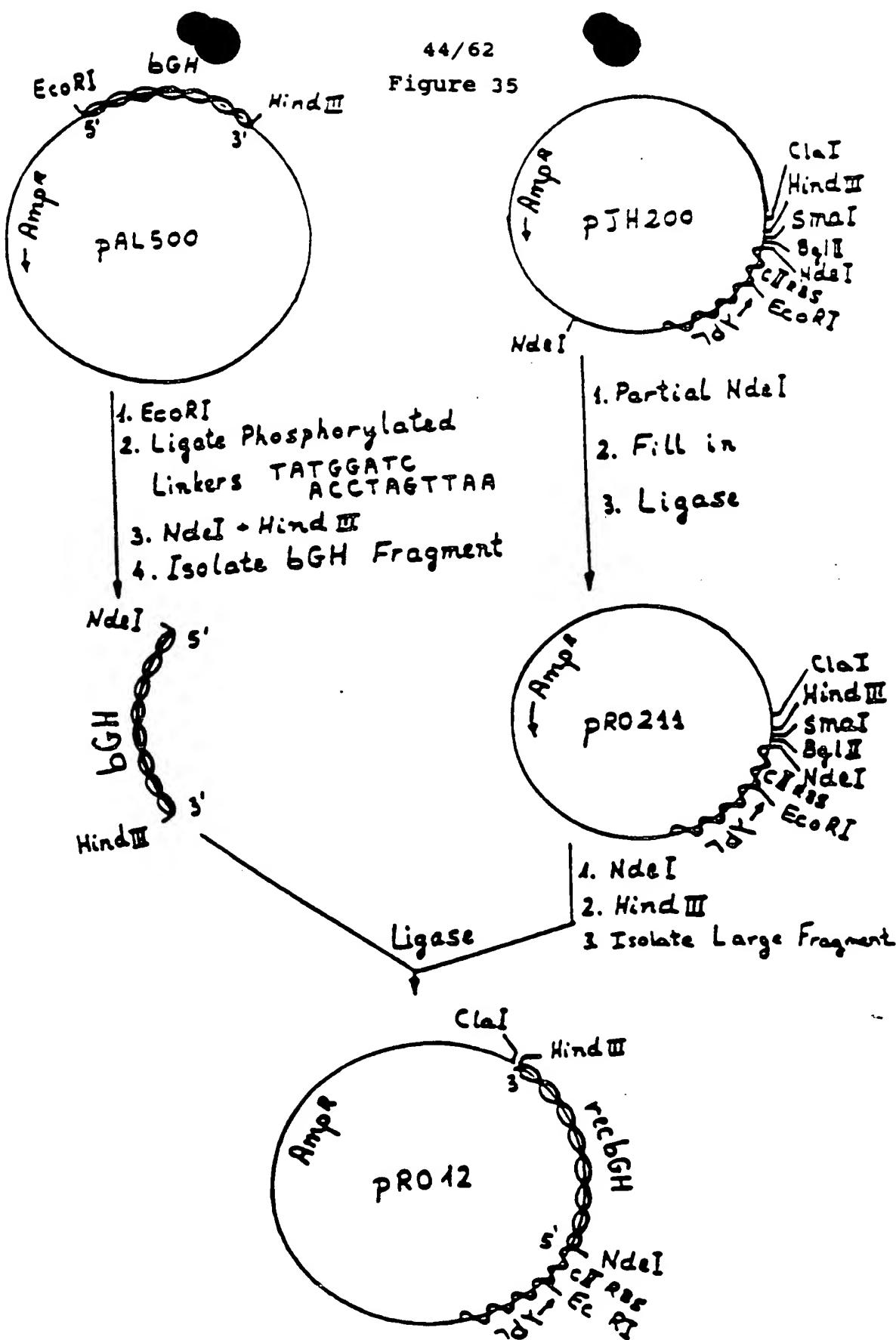
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Figur 33



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Figure 34





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Figure 36

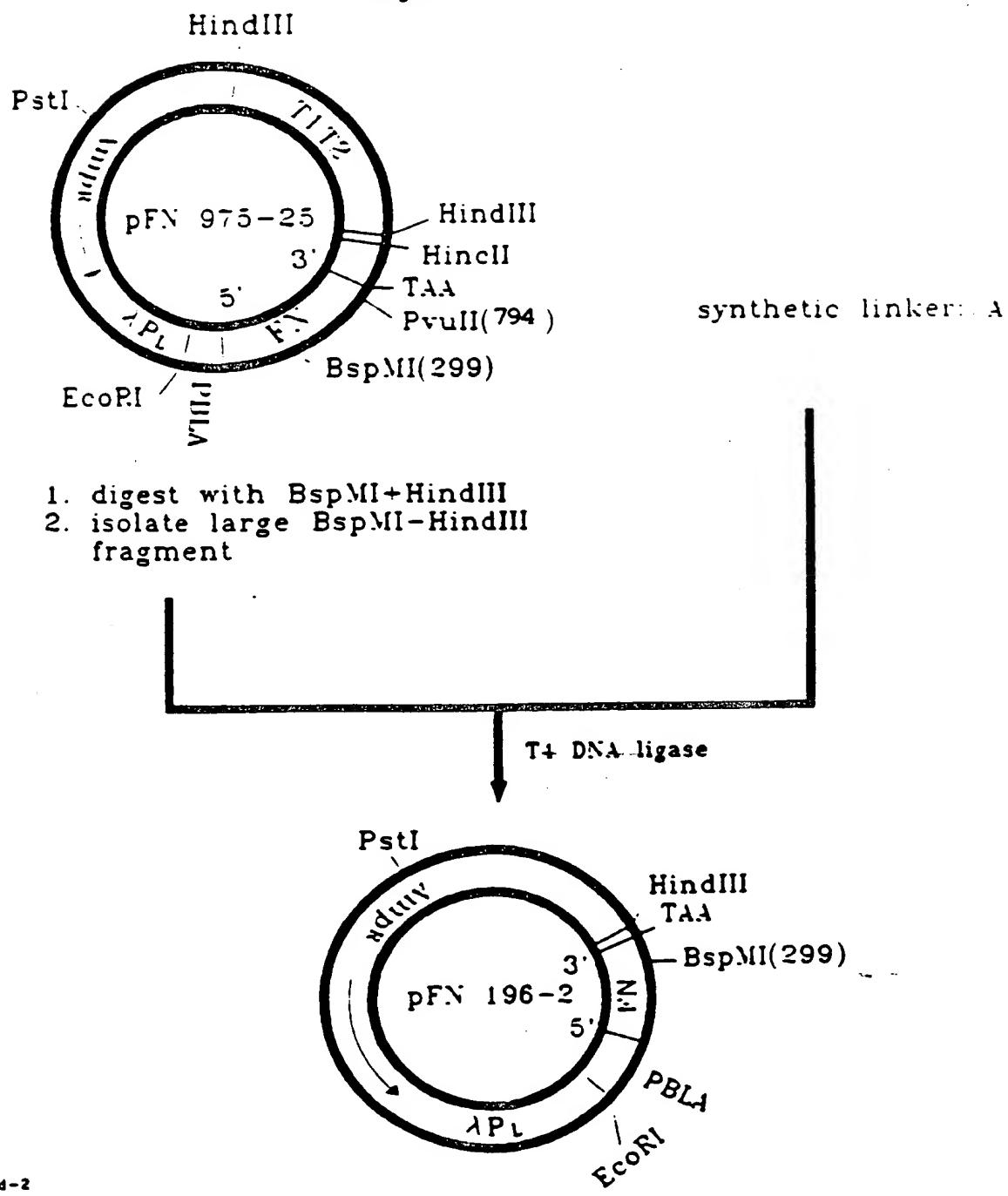


Figure 37

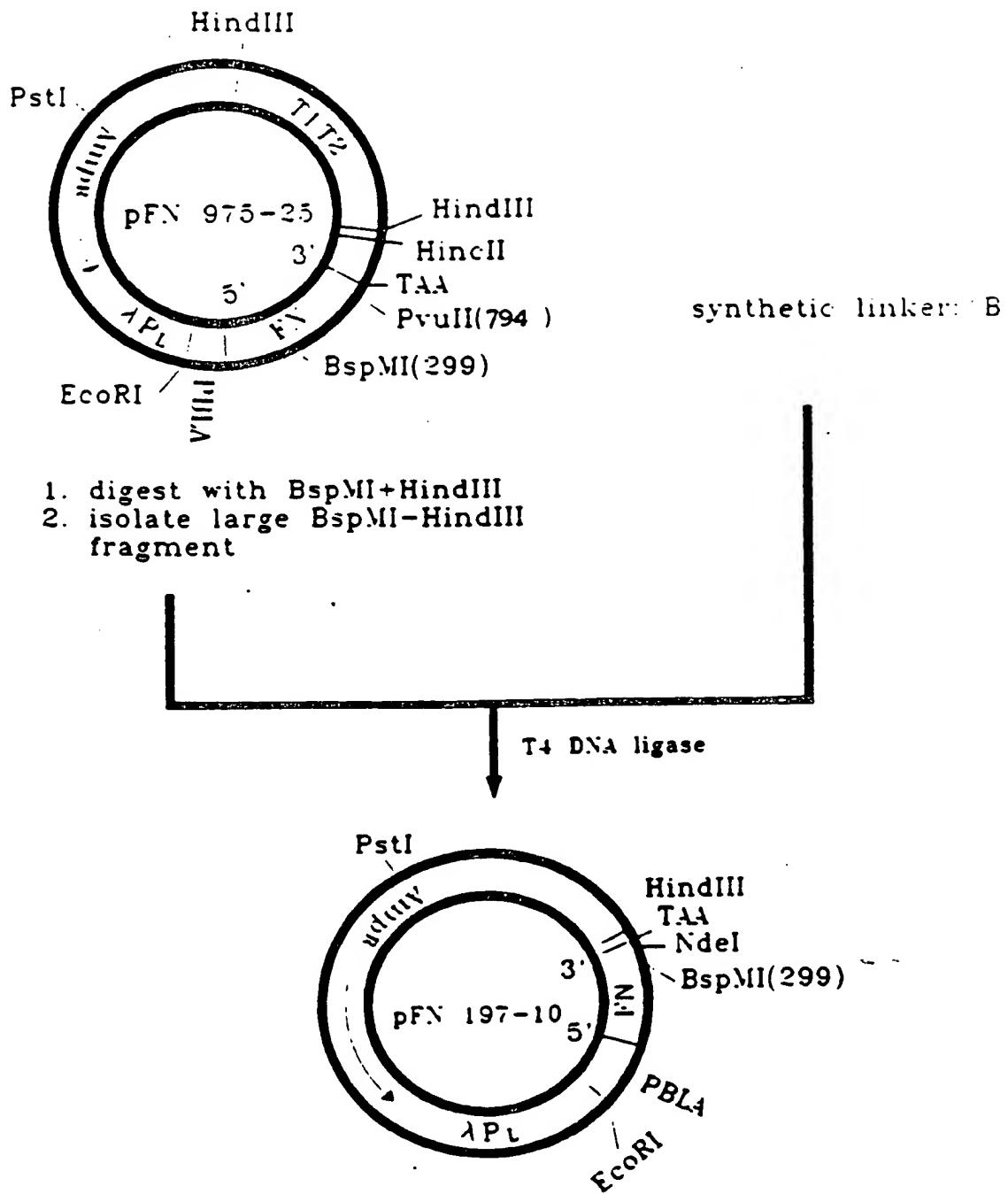


Figure 38

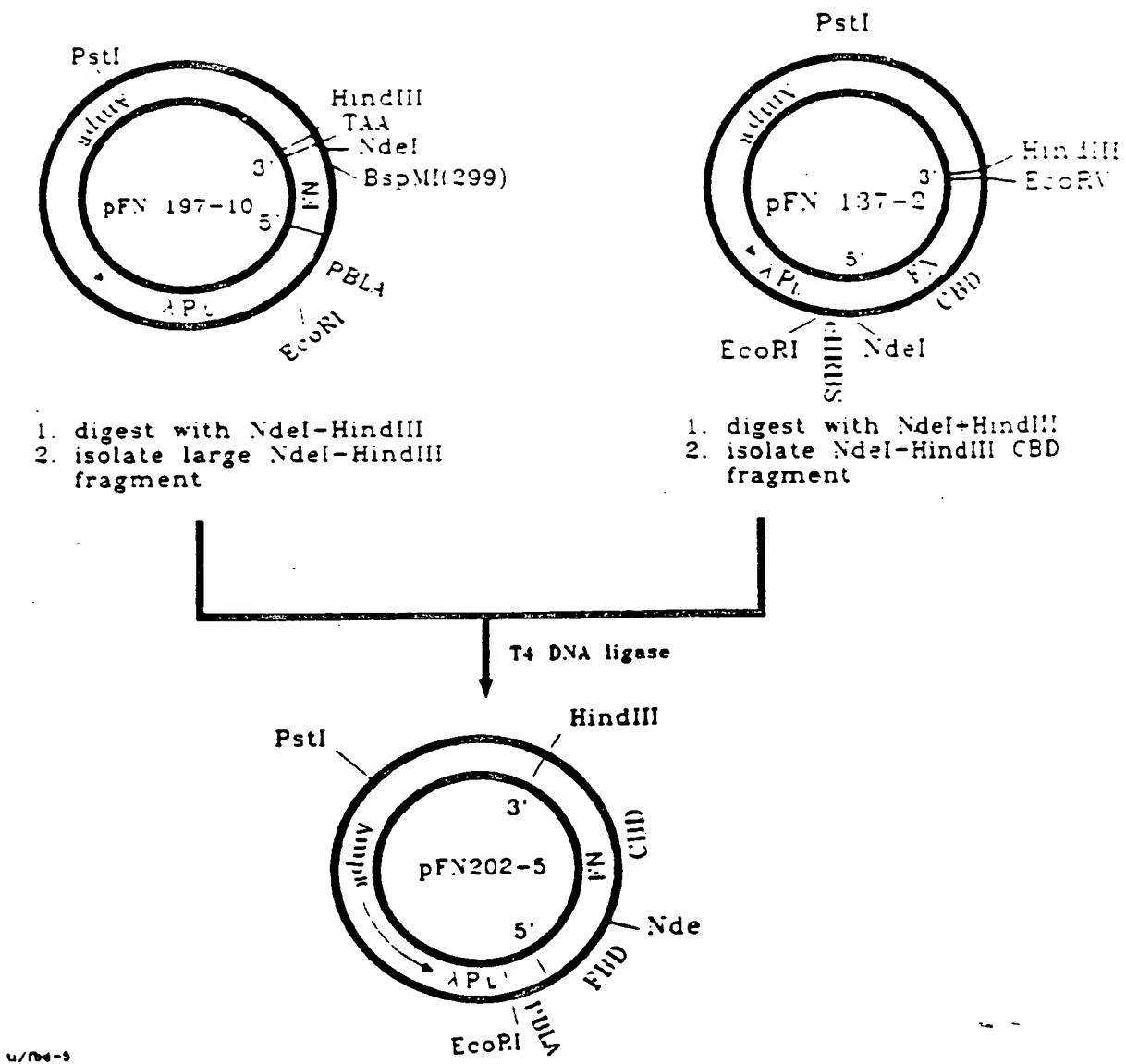
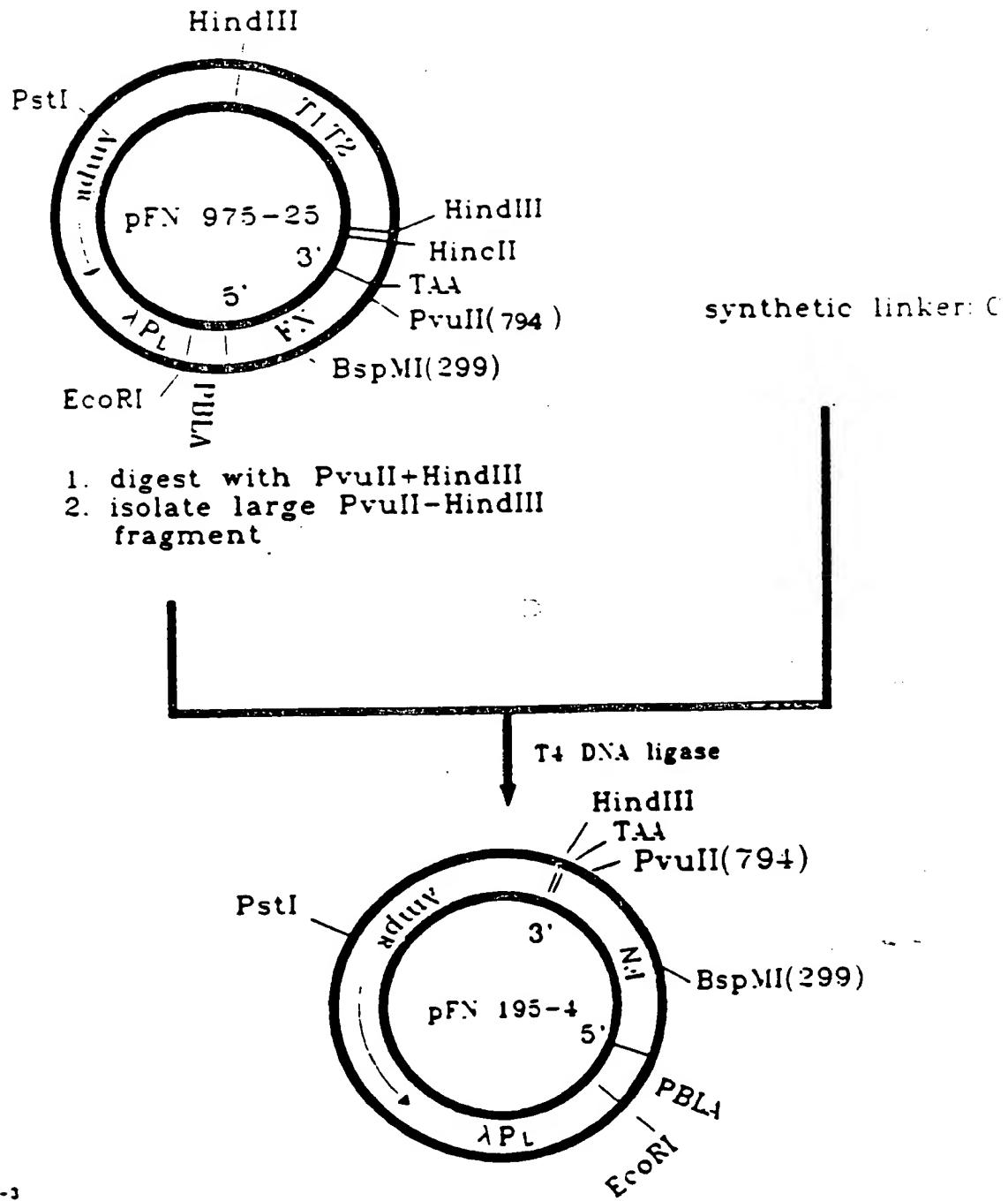


Figure 39



u/rbd-3

Figure 40

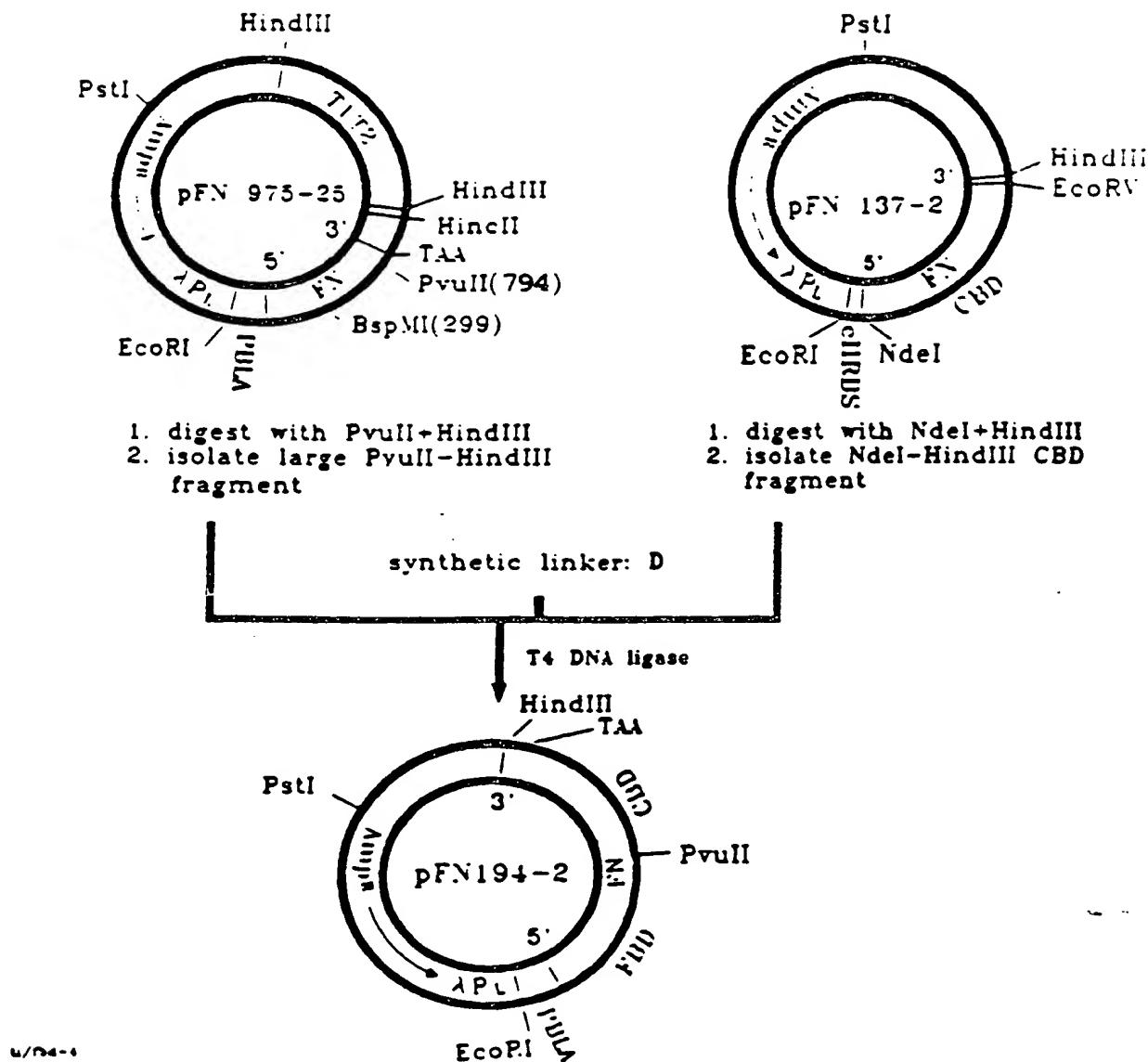


Figure 41

A 5' GGGCTGGCGAGGGAGAATAAGCTGTACCATCGCAAACCGCTAACAGCTGA 3'
3' ACCCGCTCCCTCTTATTGACATGGTAGCGTTGGCGATTGTCGACTTCGA 5'

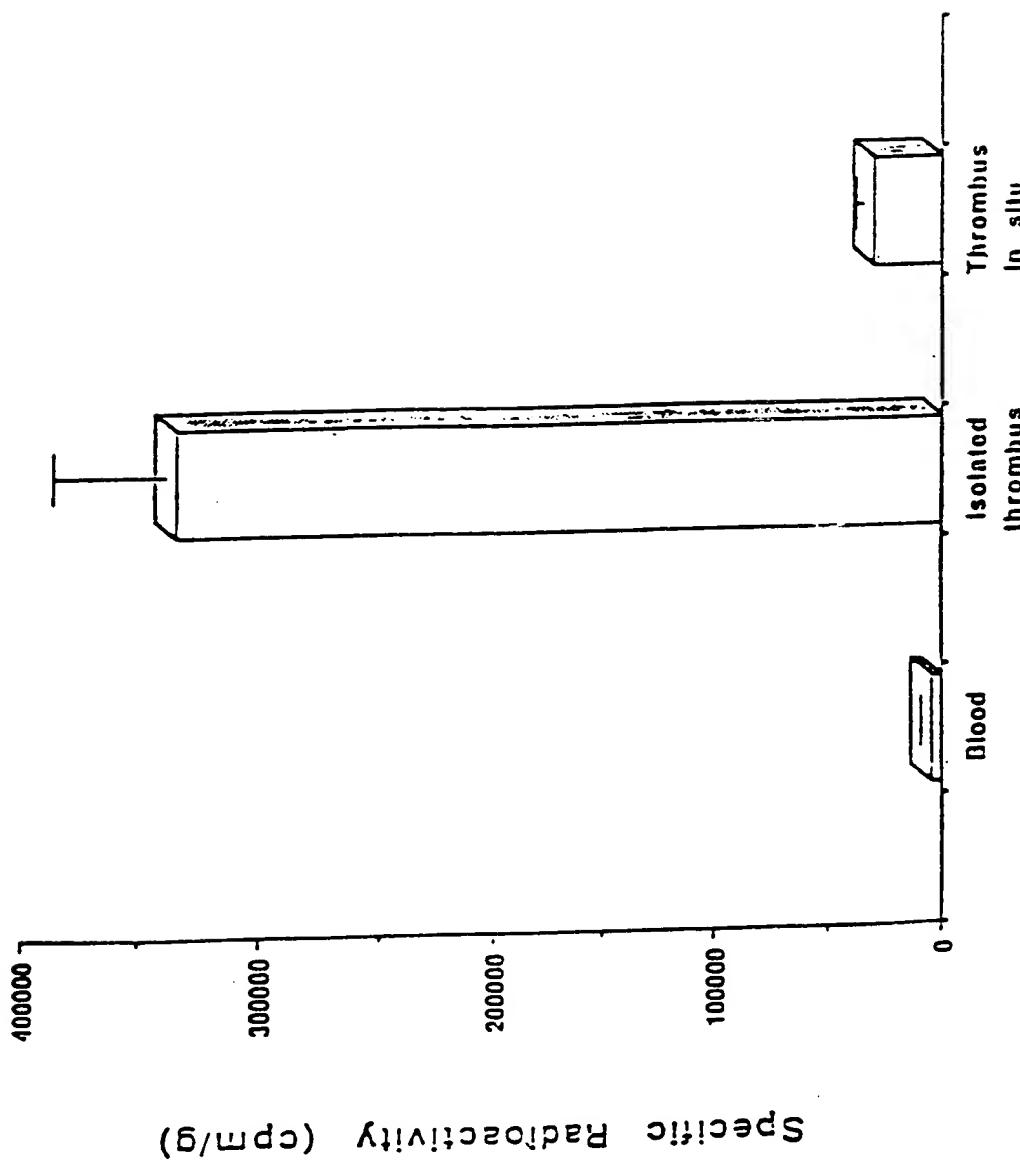
B 5' GGGCTGGCGAGGGAGAATAAGCTGTACCATCGCAAACGCCATATGTAAA 3'
3' ACCCGCTCCCTCTTATTGACATGGTAGCGTTGGCGGTATACATTTCGA 5'

C 5' ATGGCCGTGGAGACAGCTAACAGCTGA 3'
3' TACCGGCACCTCTGTCGATTGTCGACTTCGA 5'

D 5' CTGTATACCAACC 3'
3' GACATATGGTTGGAT 5'

Figure 42

Uptake of Labeled 31KD rFBD by Blood Clots in the Rat Coil Model



007217-1626460

Figure 43

COMPARISON BETWEEN 12, 20 & 31KD FBD MOLECULES

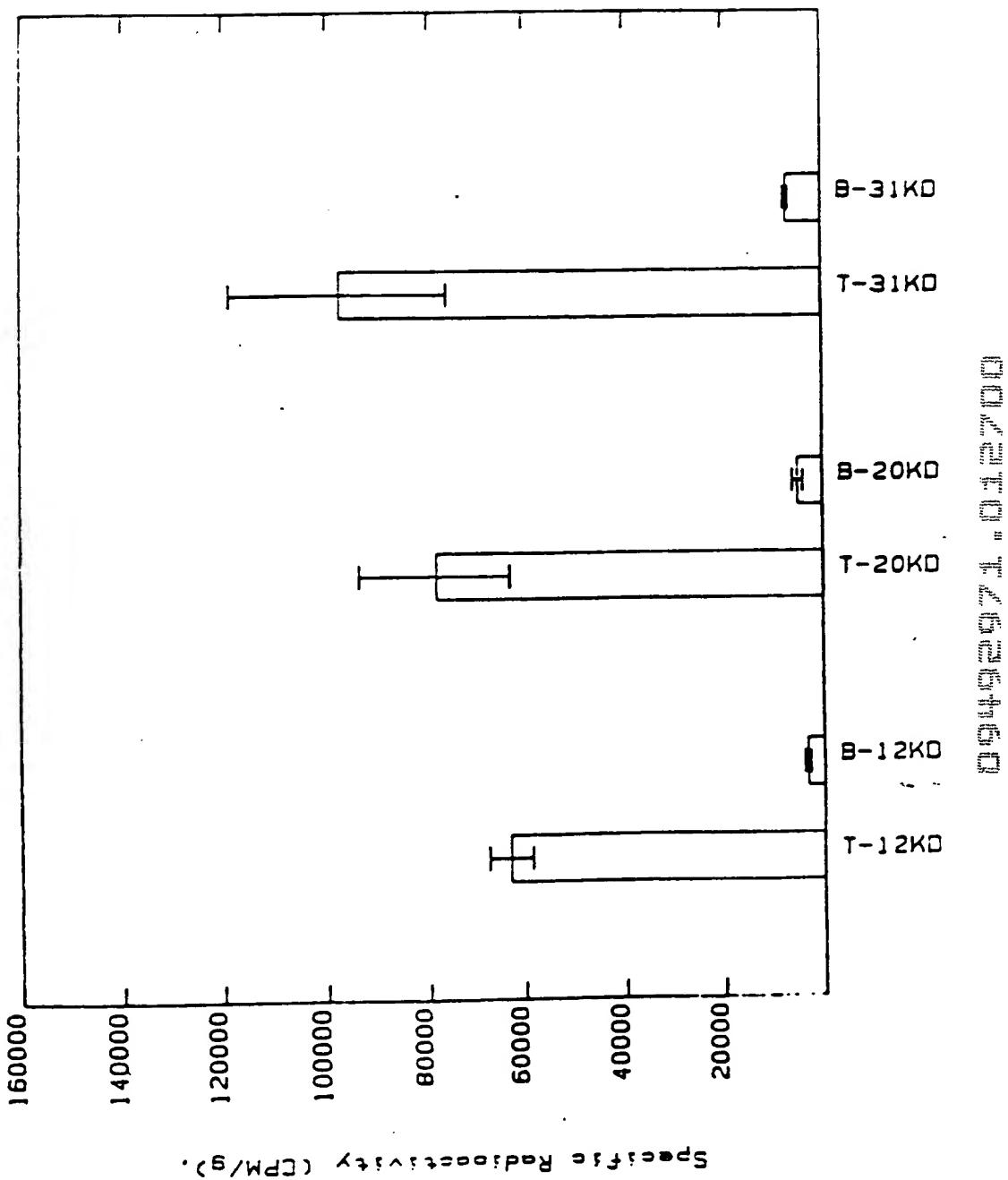
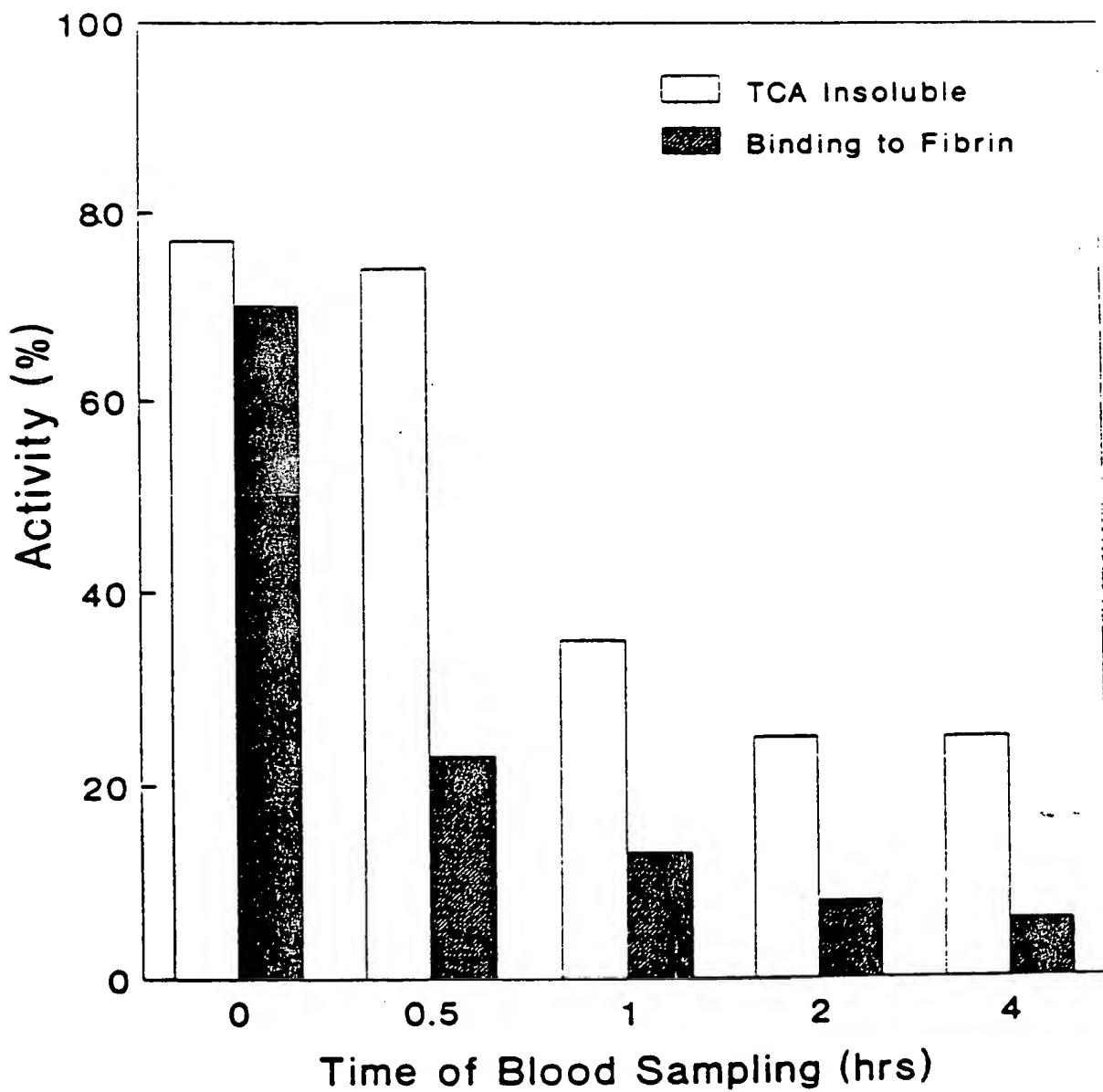


Figure 44

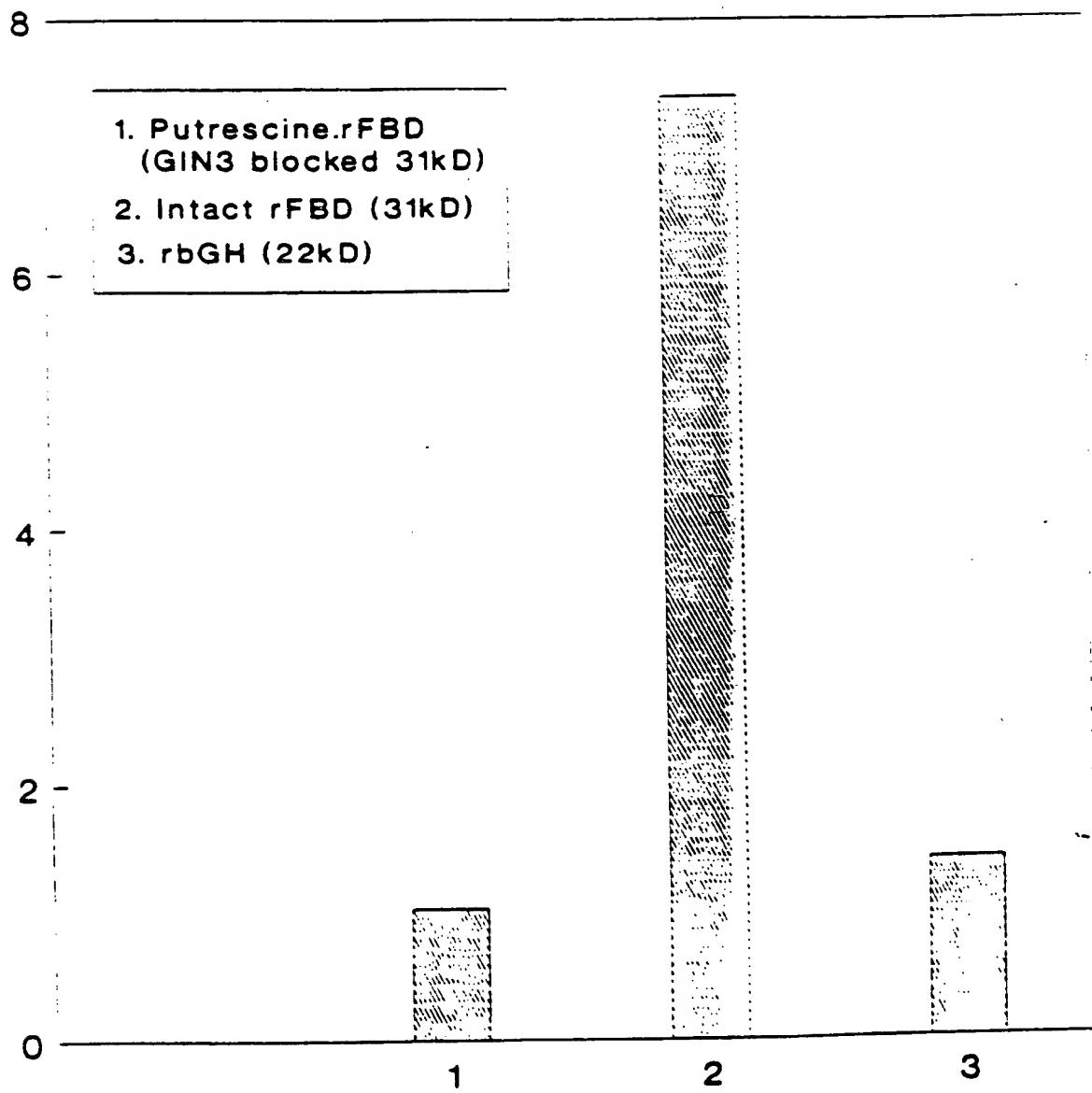
Metabolic Stability of rFBD in Rats;
Ex-vivo Binding to Fibrin vs. TCA
insolubility



ti-3/6/2

Figure 45

**Specificity of binding to Fibrin;
Effect of T.G. on the binding of
rFBD vs. rbGH (Reaction II)**



t-5

Figur 46

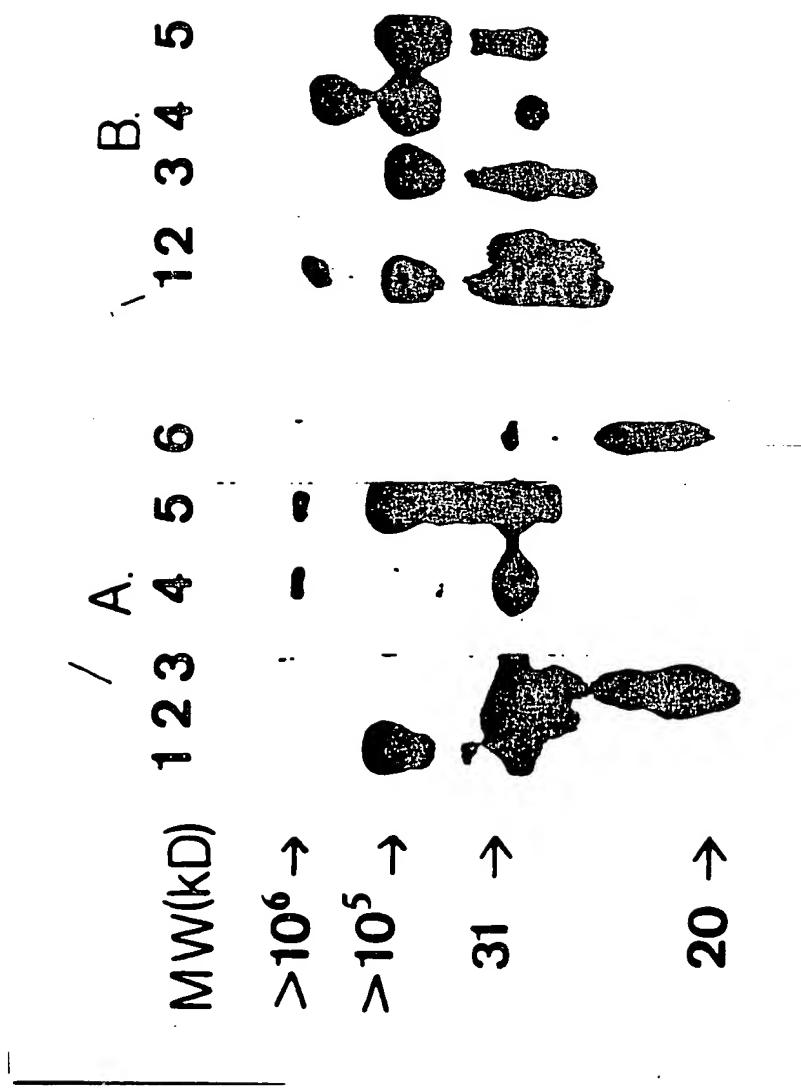


Figure 47

Binding of FBD to preformed clot (Reaction II);
Effect of FN and Heparin.

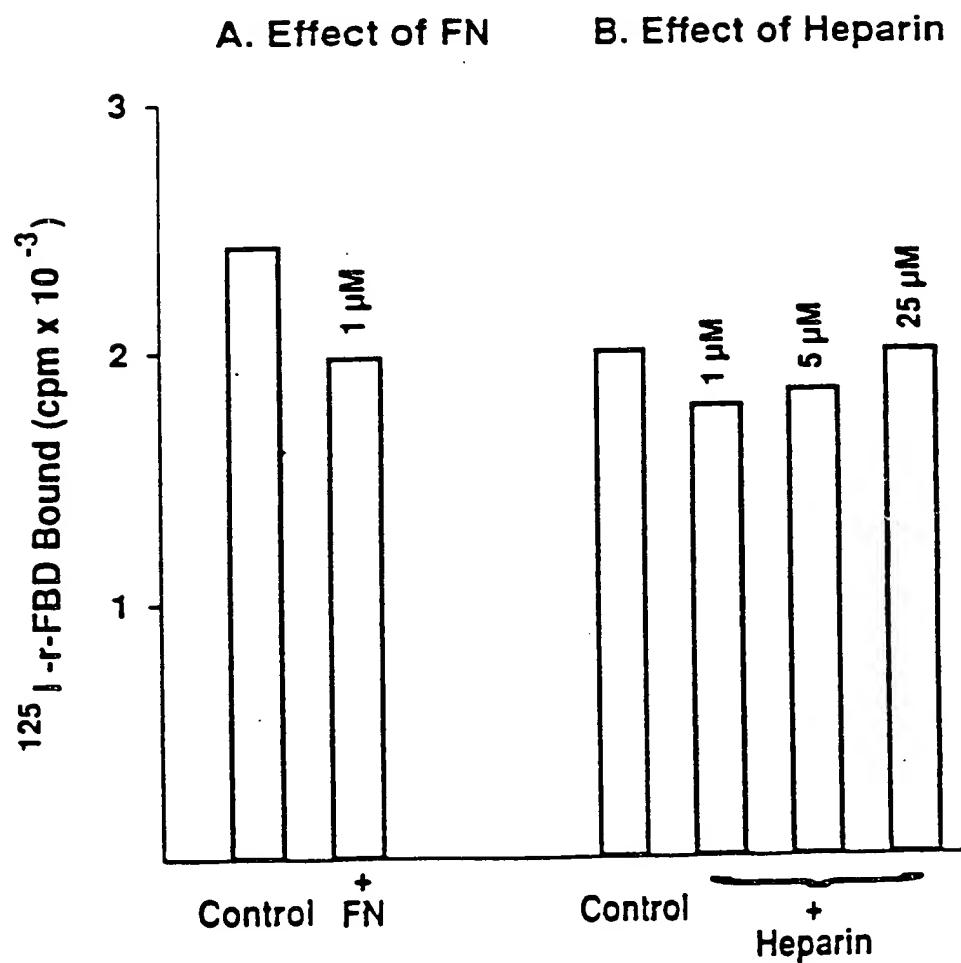


Figure 48

Binding of FBD to Fibrin clot (reaction II);
comparison between various recombinant
and plasmatic FBD molecules

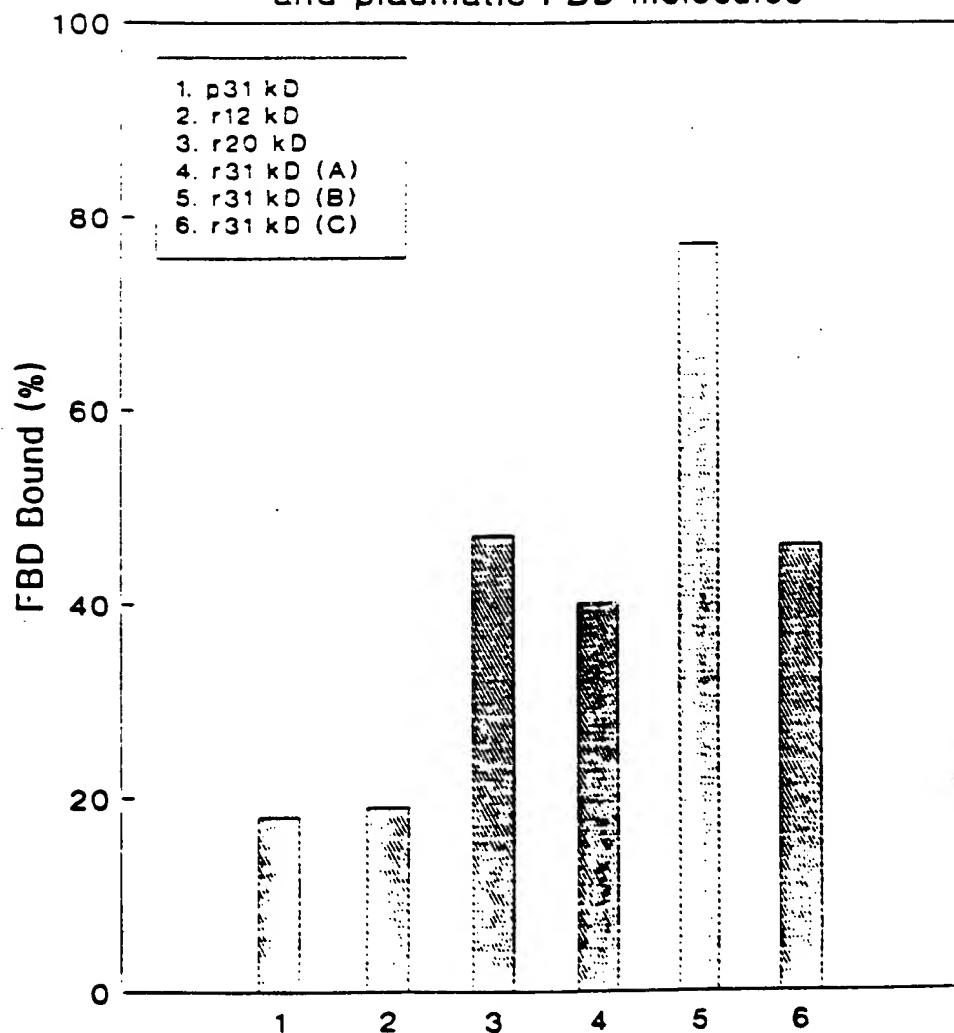
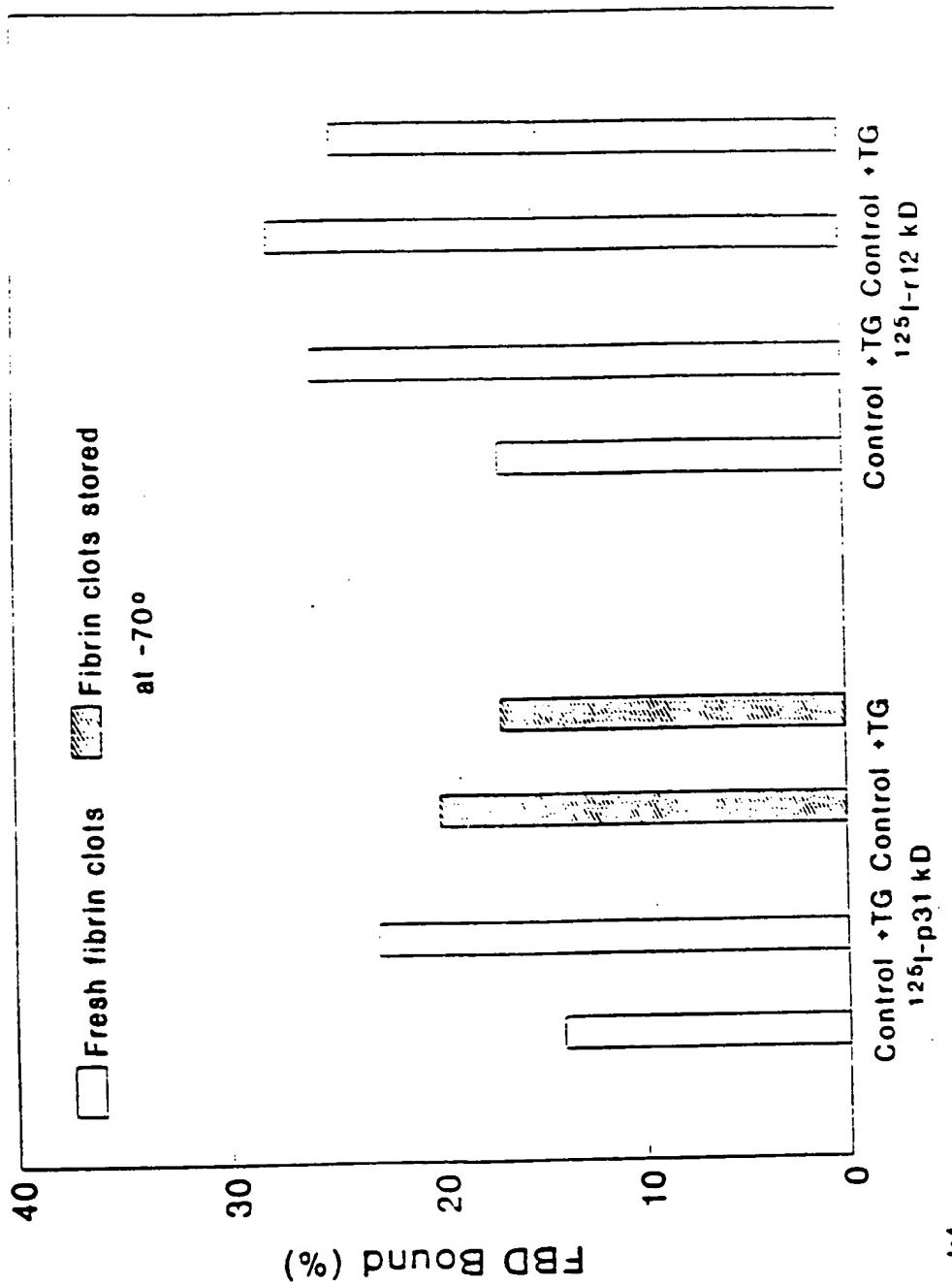


Figure 49

Binding of FBD to Fibrin clot (reaction II);
 Comparison between fresh and frozen Fibrin clots

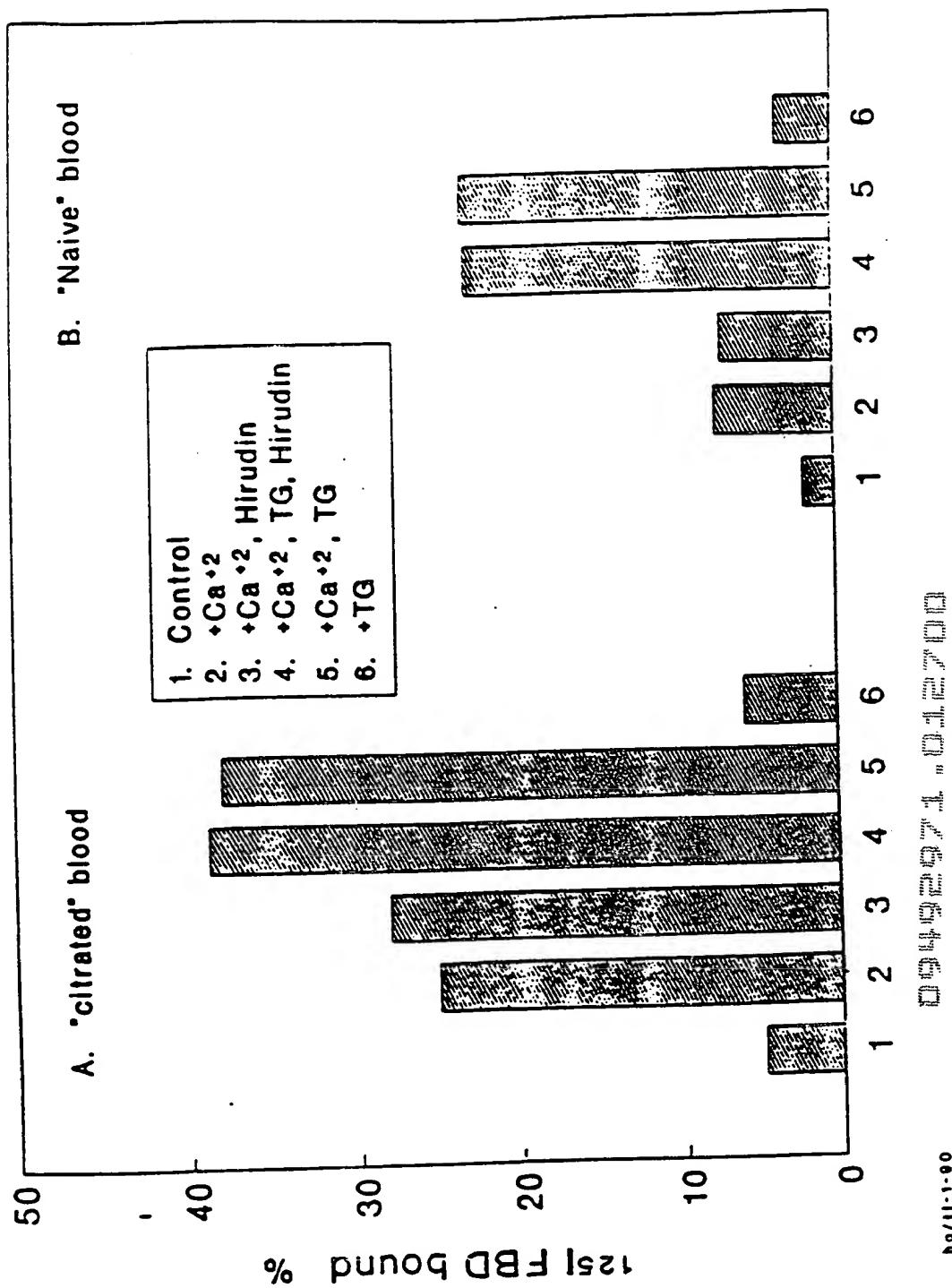


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Binding of FBD to Fibrin
(Reaction II)

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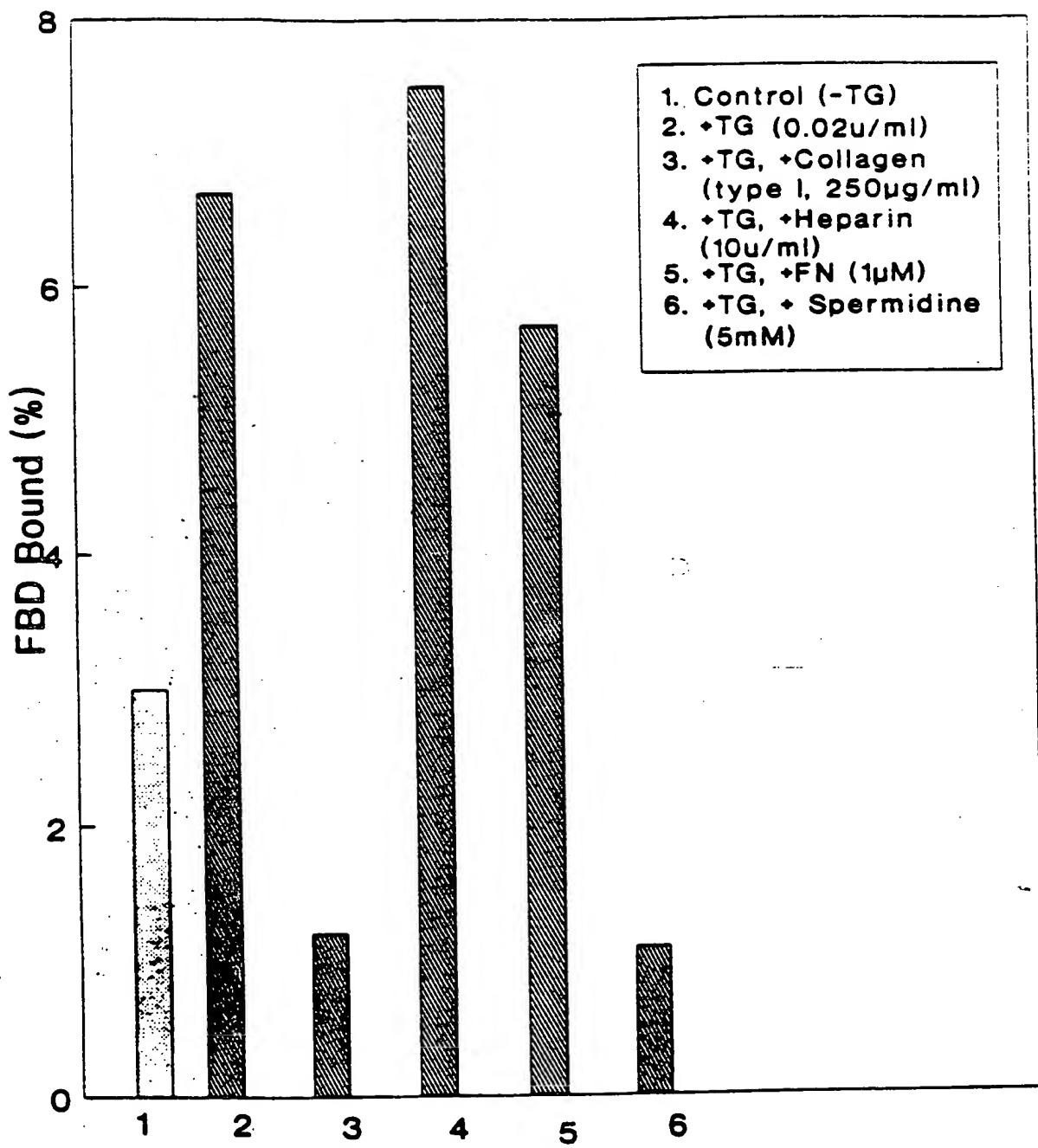
Figure 50



11-1-80

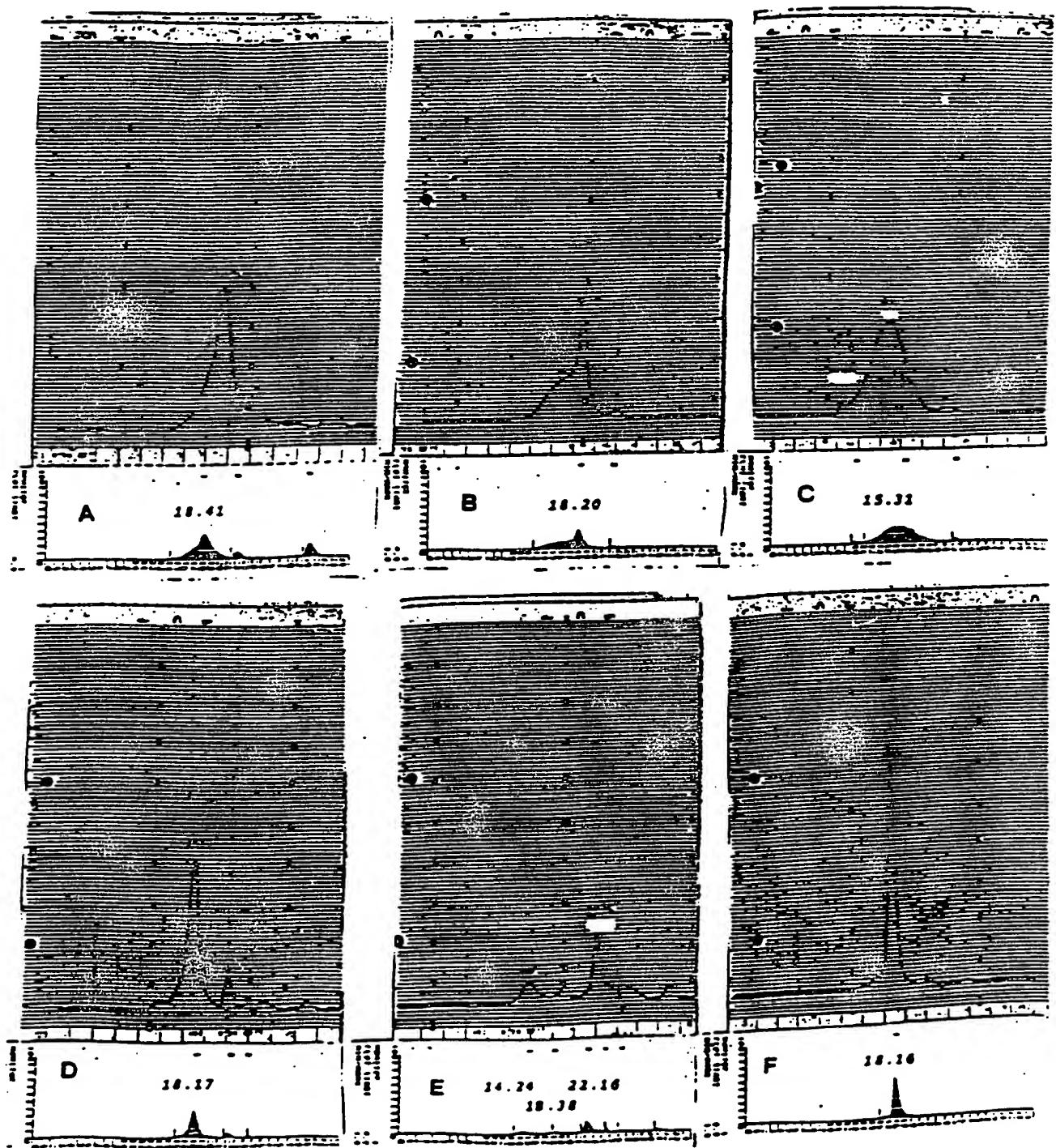
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r-FBD binding to ECM



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Figure 52



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Figure 53

